Pediatric Anterior Segment Disorders

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Anterior Segment Development

- Growth Factors
  - Insulin-like growth factor (IGF-1)
  - Fibroblast growth factor (FGF)
  - Transforming growth factor, beta (TGF-β)
- Homeobox Genes (eg. PAX6)
  - Conserved sequence of DNA
  - Control the function of other genes

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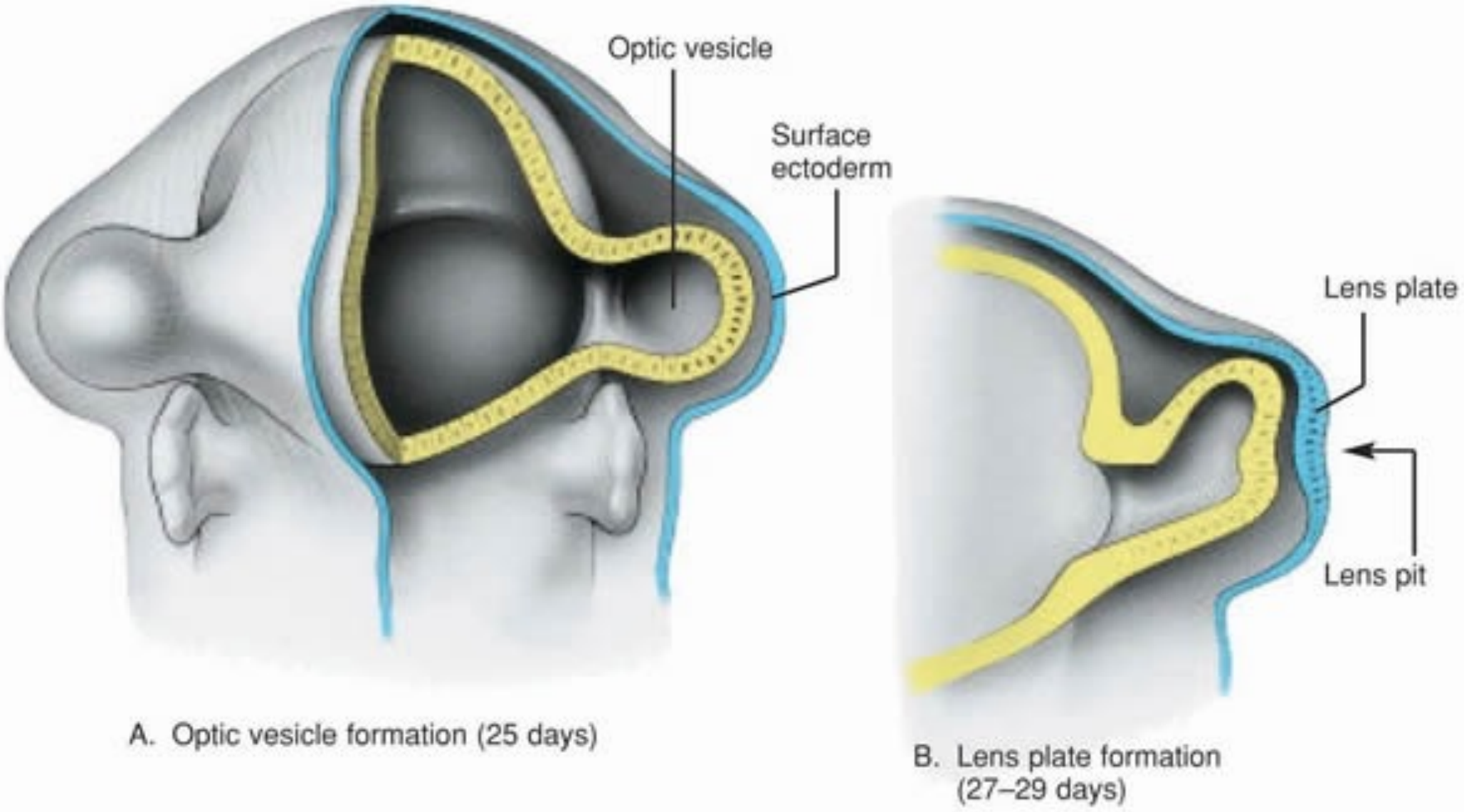
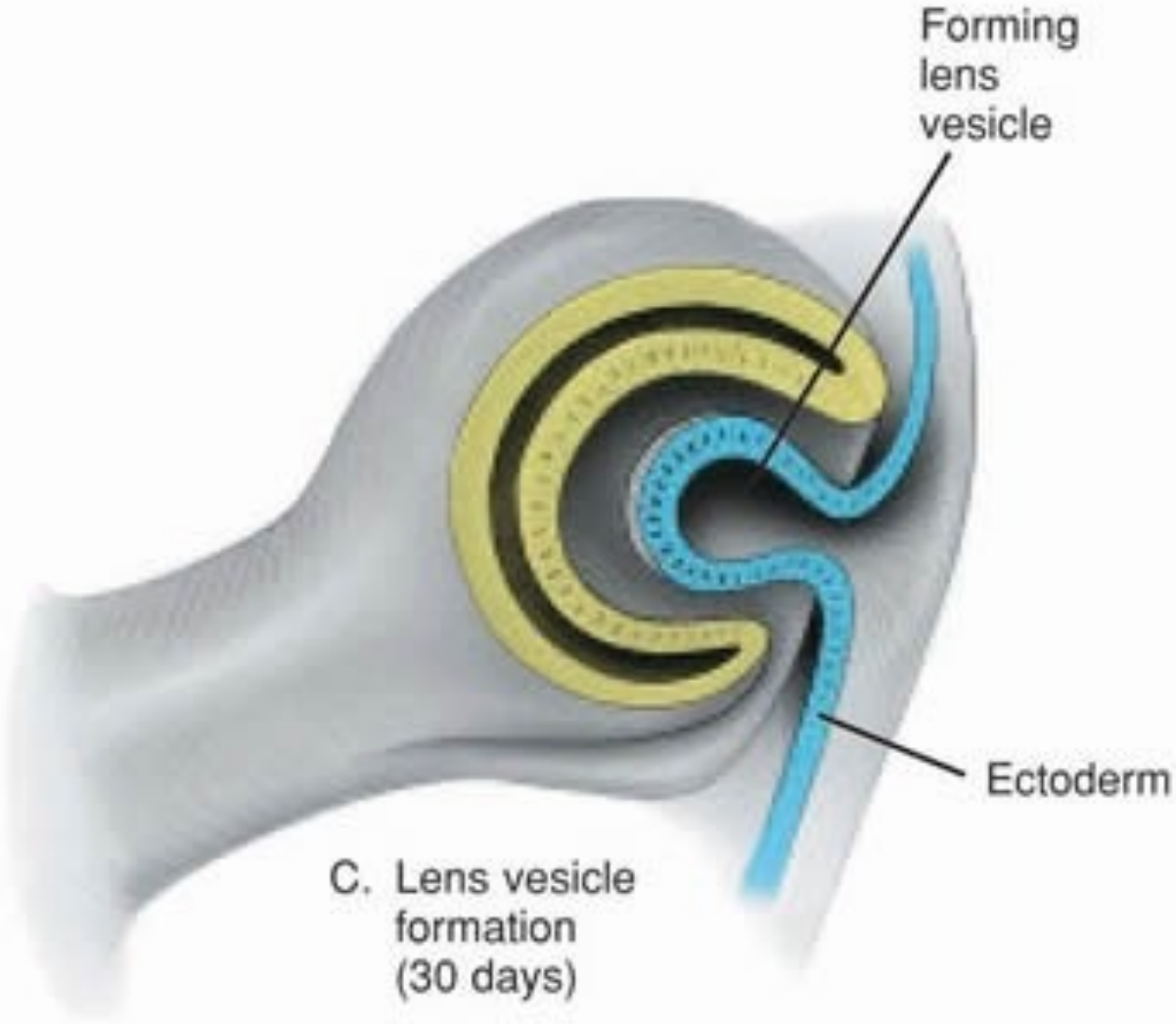
Anterior Segment Embryology

- Surface ectoderm separates from lens vesicle
  - 3 waves of neural crest cells
    - Corneal endothelium
    - Corneal stroma
    - Iris stroma and pupillary membrane
  - Endothelium overlying trabecular meshwork opens at 5 months gestation, iris root moves posterior



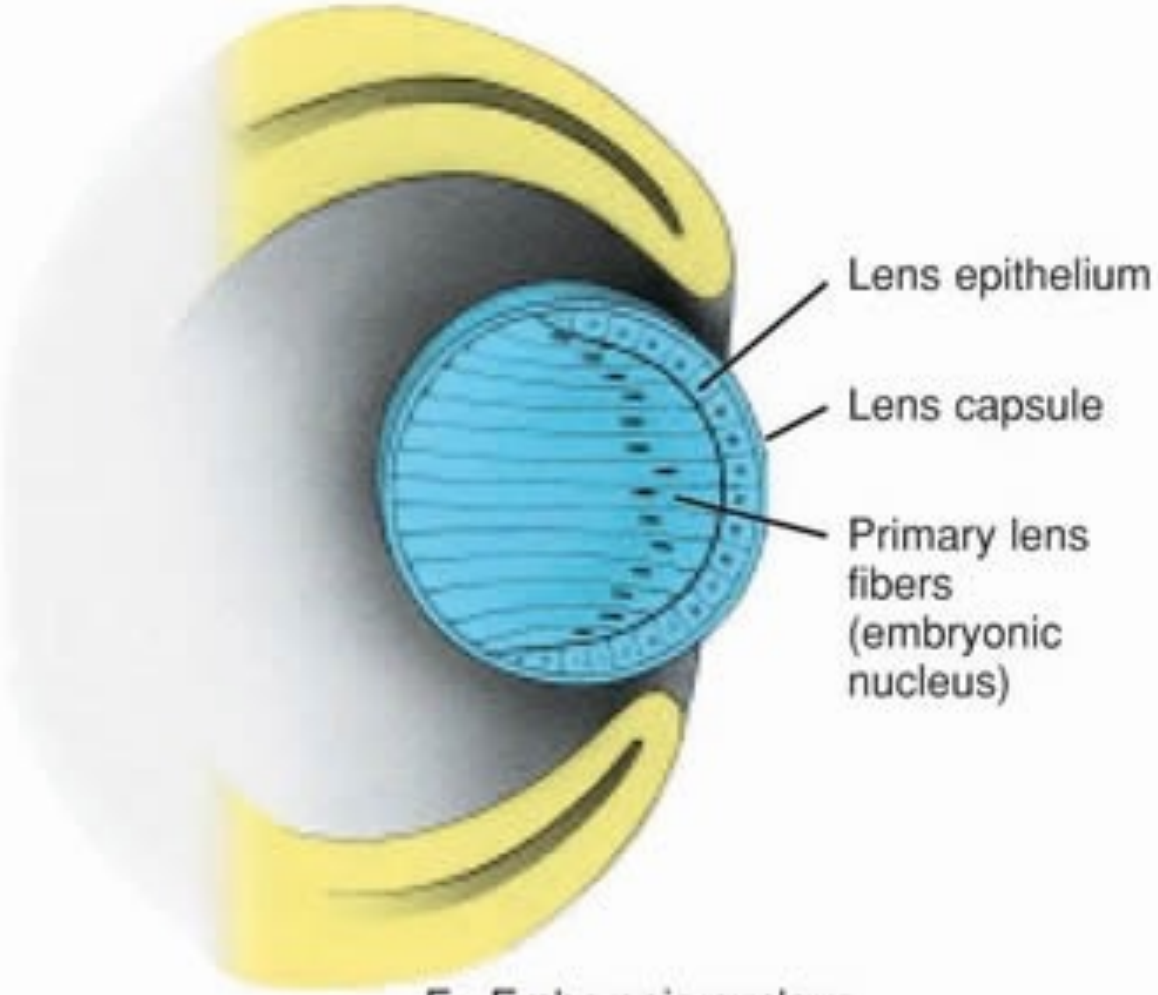
A. Optic vesicle formation (25 days)

B. Lens plate formation (27–29 days)

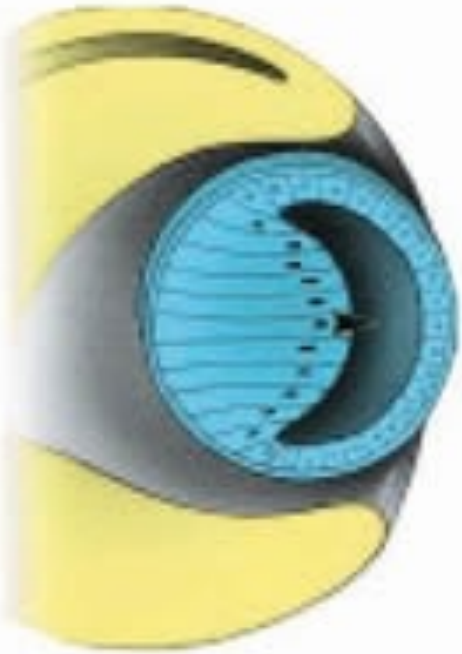


C. Lens vesicle formation (30 days)

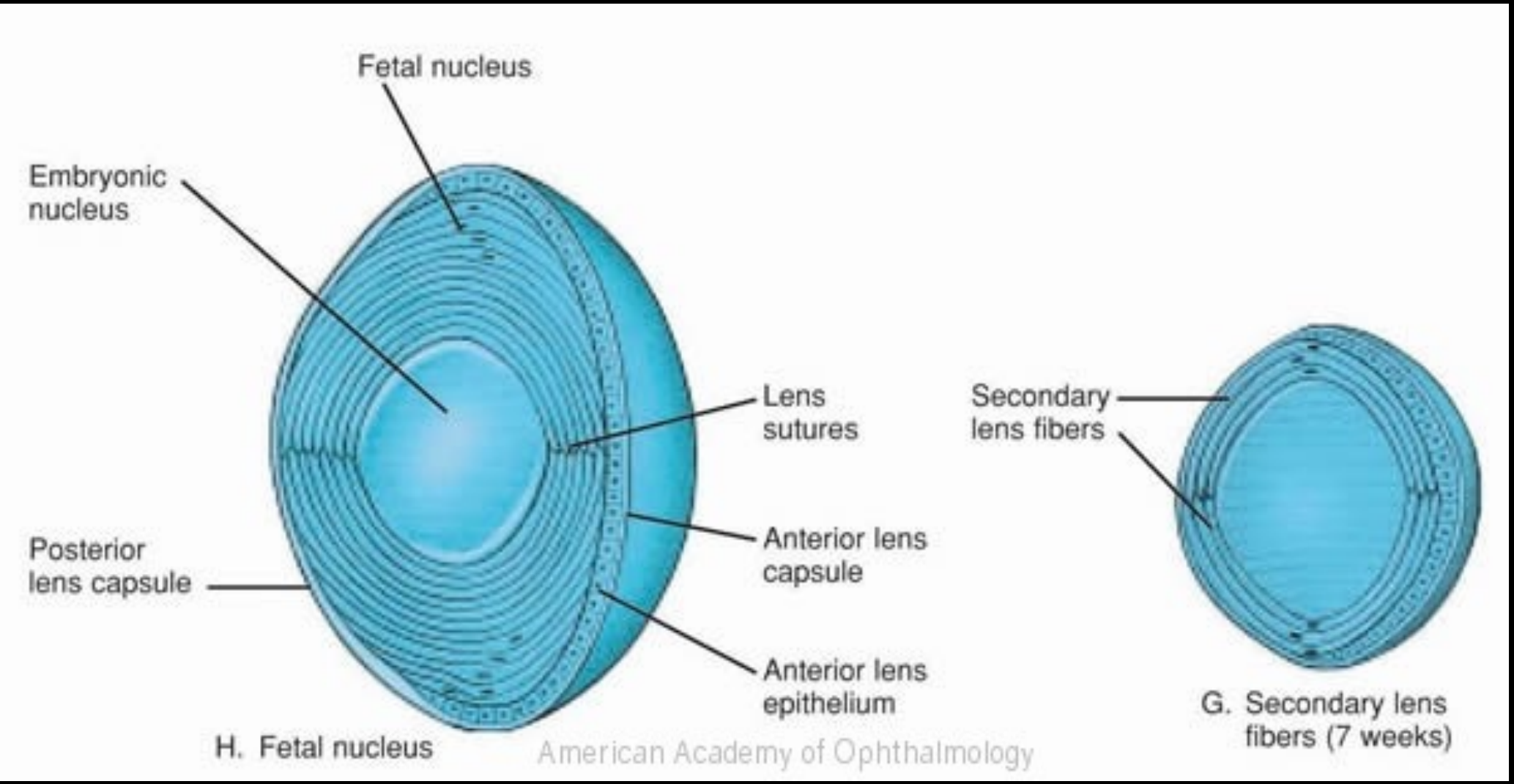
D. Lens vesicle completed (33 days)

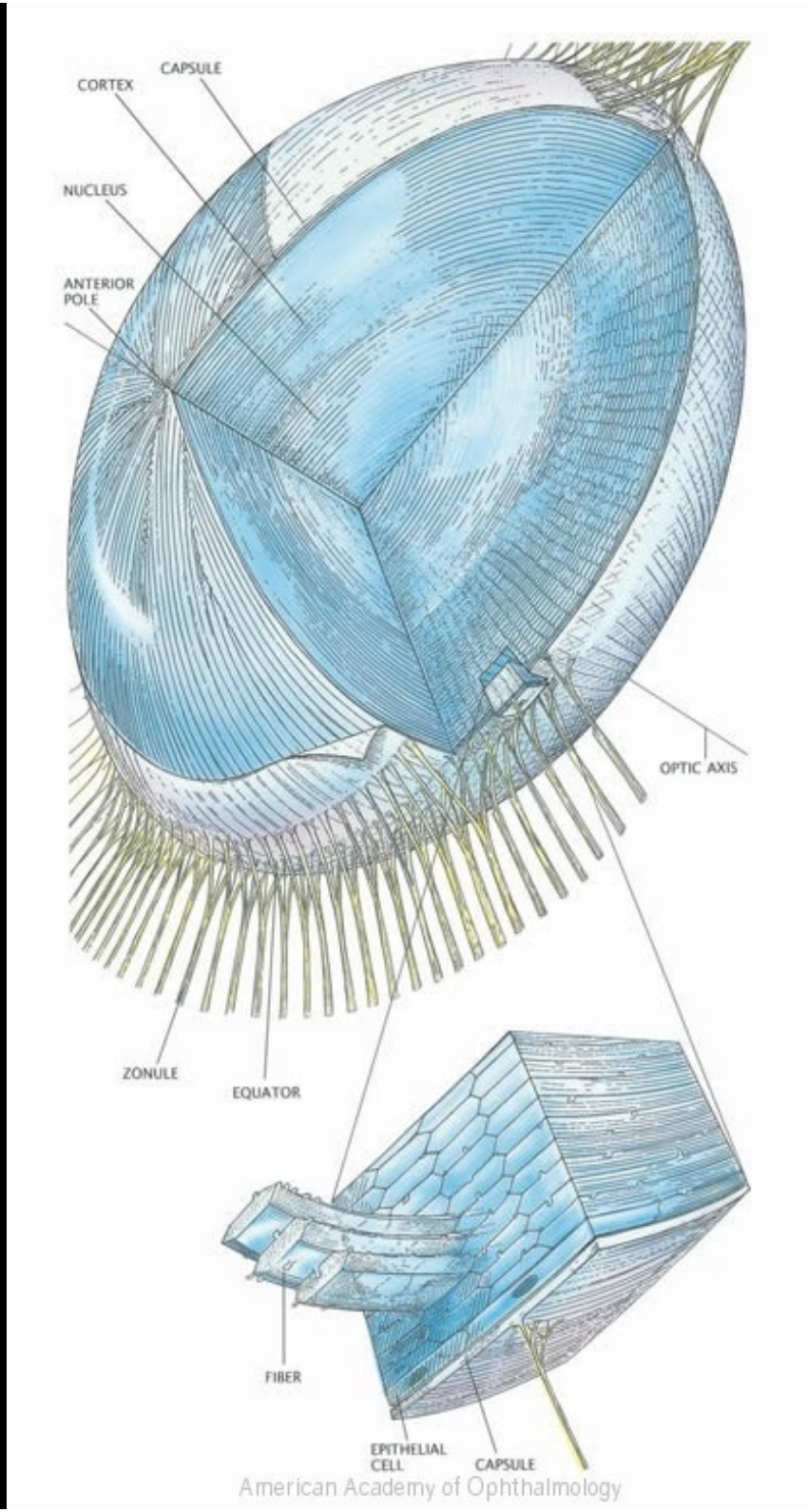


F. Embryonic nucleus formation (approximately 40 days)



E. Primary lens fibers (approximately 35 days)


Fetal nucleus
Embryonic nucleus
Lens sutures
Posterior lens capsule
Anterior lens capsule
Anterior lens epithelium
H. Fetal nucleus
Secondary lens fibers
G. Secondary lens fibers (7 weeks)
American Academy of Ophthalmology



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Malformations/Diseases

- Cornea
  - Size/Shape
  - Dysgenesis
  - Opacities
  - Systemic Diseases
- Iris
  - Structure
  - Pupillary membranes
  - Cysts
- Trabecular meshwork: Glaucoma
- Lens
  - Dislocation/Subluxation
  - Cataracts

- Pages 249-310 BCSC Pediatric Ophthalmology and Strabismus

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Pediatric Corneal Abnormalities

- Normal newborn corneal diameter
  - 9.5-10.5 mm
- Adult corneal diameter by age 2
  - 12mm

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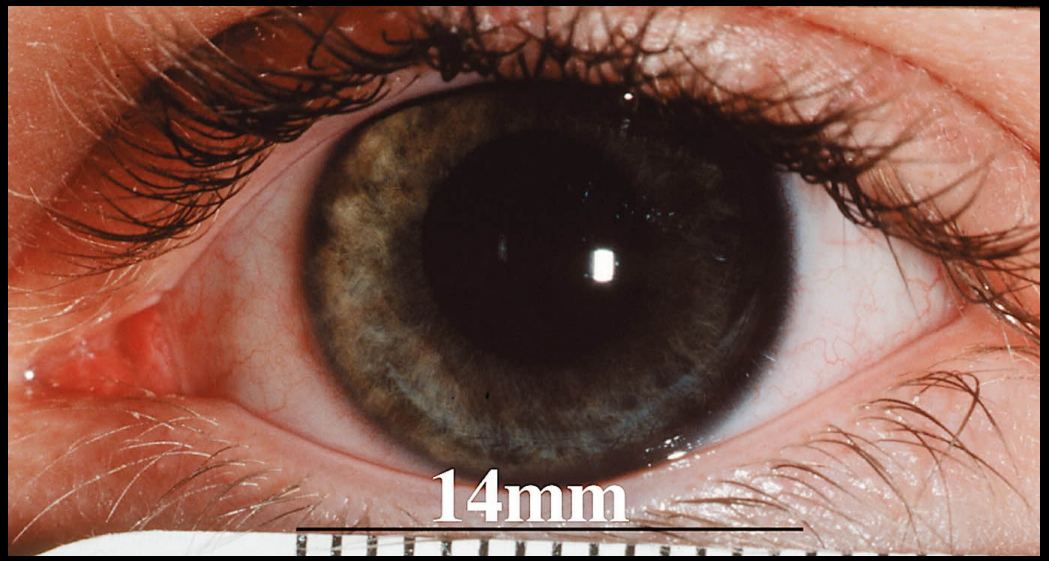
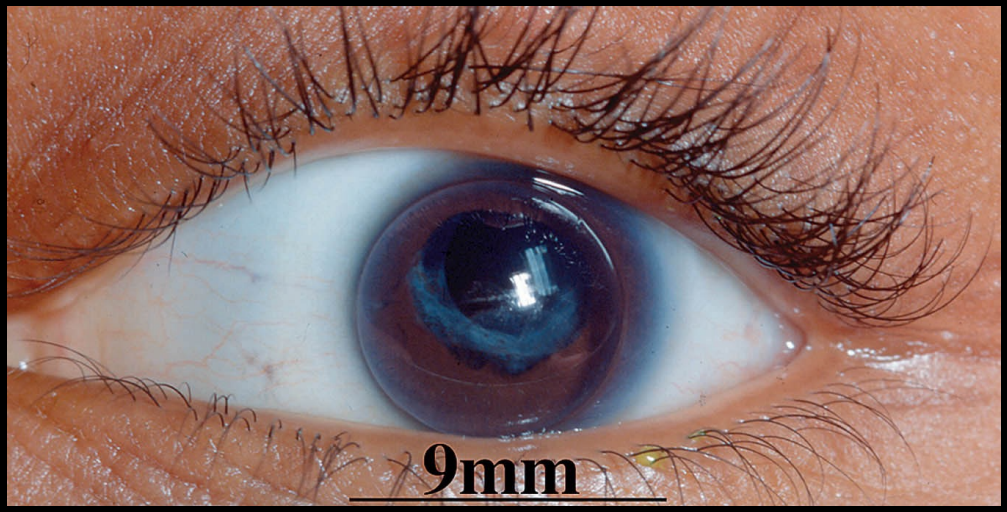
Megalocornea

- Corneal diameter > 12mm in newborn, or >13 in child over two
- Bilateral
- Anterior megalophthalmos
  - Most common is X-linked recessive
  - Lens is normal size but ciliary ring is large-lens subluxation possible
  - Iris thin and pupil often misplaced
  - Risk of Glaucoma 50%
- Simple Megalocornea
  - Rare
  - No glaucoma



Microcornea

- Corneal diameter <9mm in newborn or 10mm in older than 2



- Sporatic
- Autosomal dominant
  - Oculodentaldigital syndrome
- May occur with microphthalmos, PHPV or other ocular abnormalities

Globe Size

- Microphthalmia
  - Axial Eye length >2 SD below the mean for age:
    - Normal Neonate: 17 mm (<16.5mm)
    - Normal Adult: 24 mm (<22mm)
  - Simple Microphthalmos. Arch Ophthalmol. 1989 Nov;107(11):1625-30
  - Refractive development of the human eye Arch Ophthalmol. 1985 Jun;103(6):785-9.
- Nanophthalmos
  - normal eye structures but eye smaller than normal
  - Associated with secondary glaucoma later due to lens growth

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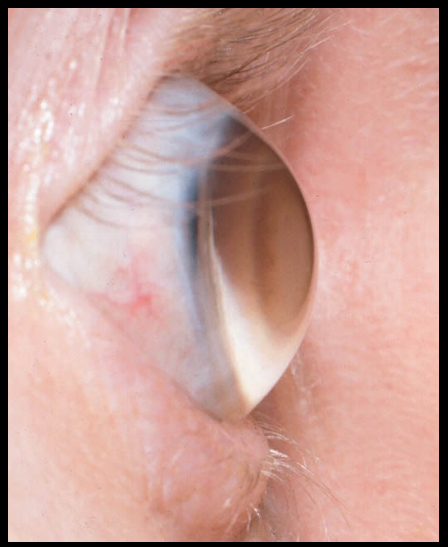
Keratoglobus

- Thinner cornea with high arch configuration
- Deeper than normal anterior chamber
- May have spontaneous corneal edema from Decemet's breaks
- Cornea may rupture from blunt truma
- Eye protection
- Ehlers-Danlos VI
  - Hyperextensible joints, blue sclera, progressive neurosensory hearing loss, keratoglobus



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Keratoconus

- Central and paracentral cornea thins and protrudes taking on shape of cone, usually begins early to mid teens.
- Can be entire corneal thickness or just posterior surface
- Rarely begins in childhood except posterior variety, usually first seen in adolescence
- Early sign: progressive astigmatism
- More common in Down Syndrome and other conditions with mental retardation, and atopic disease
- More common with family history

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Pediatric Corneal Opacities S.T.U.M.P.E.D.

- #1 GLAUCOMA *****

- Sclerocornea
- Trauma
- Ulcers (sterile or infectious)
- Mucopolysaccharidoses, mucolipidoses
- Peter's anomaly
- Endothelial dystrophy (CHED)
- Dermoid

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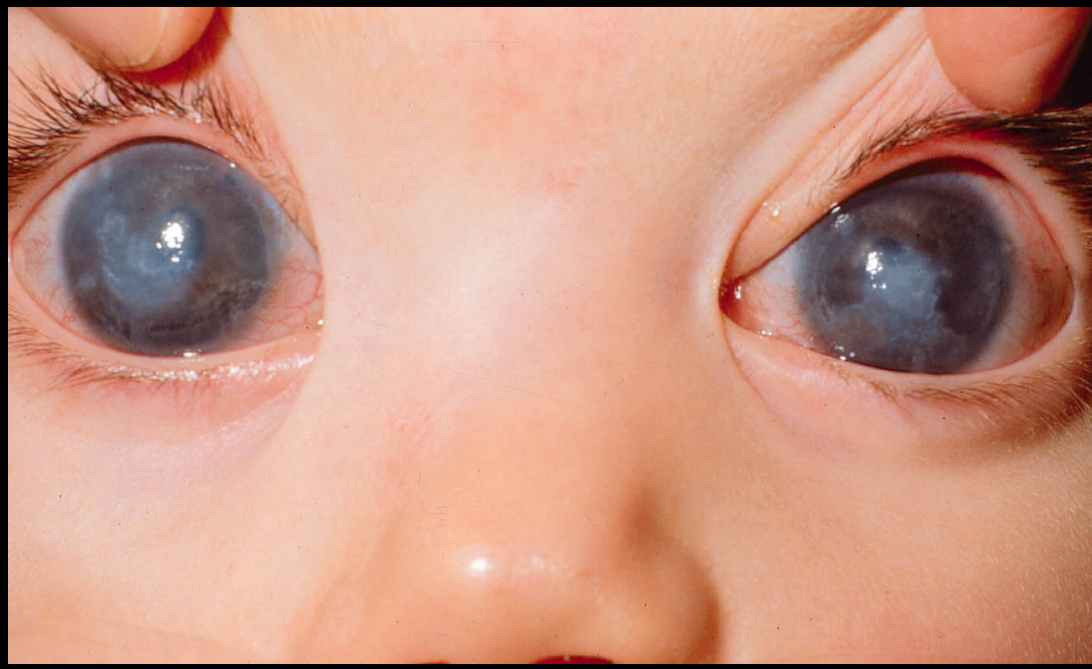
Primary Infantile Glaucoma

- 1/10,000
- Defect in trabecular meshwork
- Responds to “angle” surgery
- Triad of symptoms
  - Photophobia
  - Tearing
  - Blepharospasm



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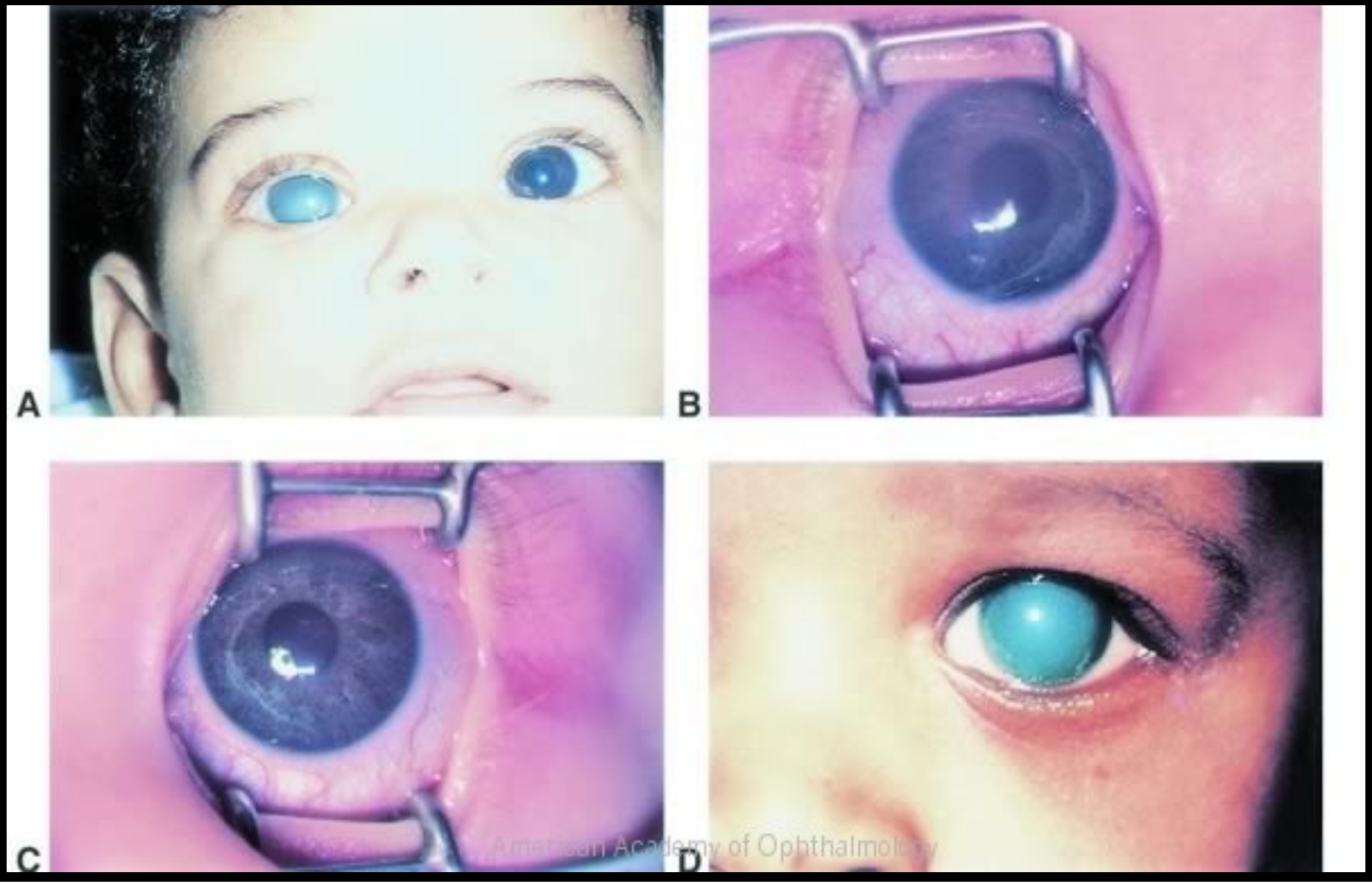
Congenital Glaucoma- signs



Sclerocornea

- Congenital absence of limbal transition
- Relative clearing of central cornea, cornea very flat
- Recessive forms more severe, Dominant less so
- Often associated with other ocular abnormalities
  - Microphthalmia
  - Optic nerve hypoplasia or agenesis

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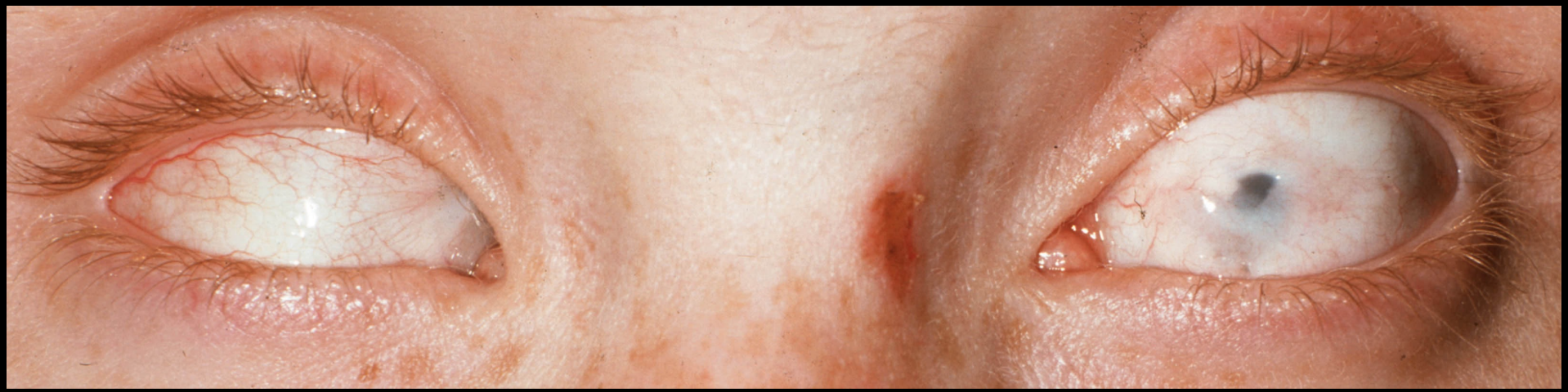
Sclerocornea

- Lack of limbal differentiation
- Corneal transplants inevitably fail
- Glaucoma common
- Vision usually poor if any



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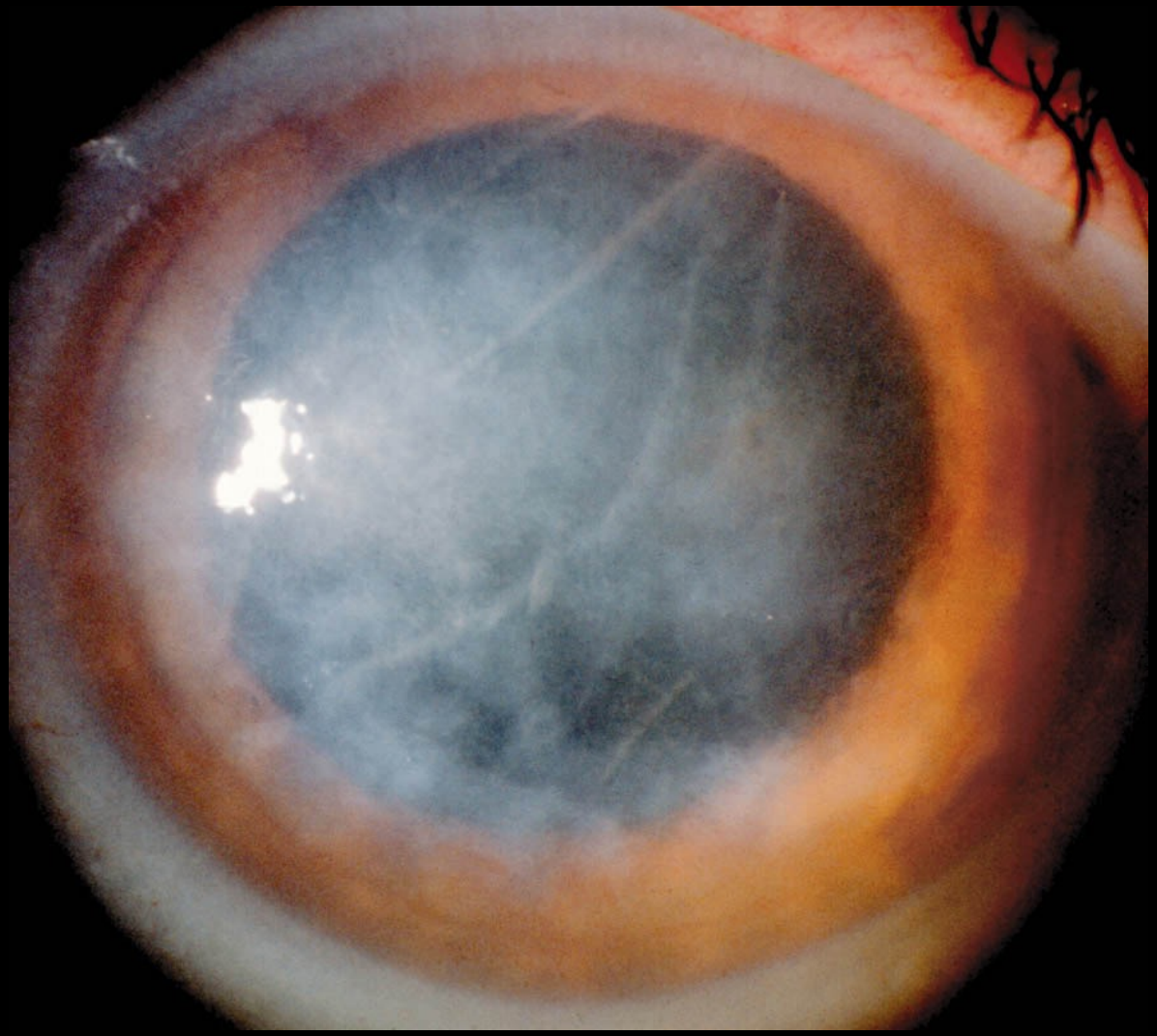
Forceps Injury



Keratitis

- Intrauterine syphillis
  - Inflamed eye with corneal clouding
  - Late signs: Deep stromal vascularization, Iris atrophy, and corneal scarring
  - Hutchinson's teeth/ saddle nose
- Intrauterine rubella
  - Transient corneal edema
  - episcleral injection
  - typically a nuclear cataract
  - increased intraocular pressure
  - posterior synechiae
  - miosis.

Mucopolysaccharidoses/ Mucolipidosis

- 3 lysosomal disorders that have corneal clouding early in life
  - Mucopolysaccharidosis IH (Hurler)
    - Clouding by 6 months
  - Mucopolysaccharidosis IS (Scheie)
    - Clouding by 12-24 months
  - Mucolipidosis IV
    - Clouding by 6 weeks possible
- Systemic signs: normal at birth, then growth falls off, hepatosplenomegaly, development delays

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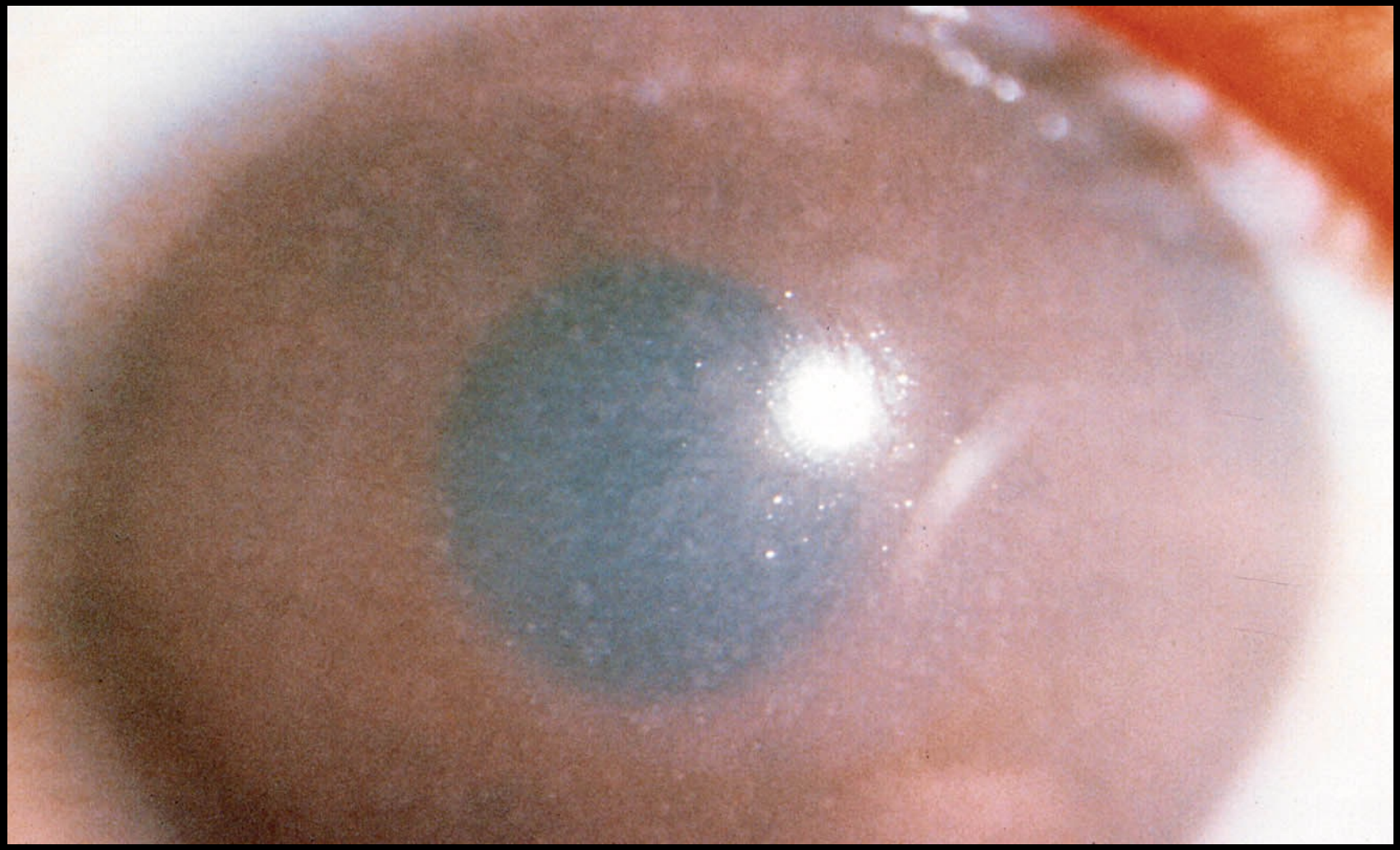
Hurler Syndrome



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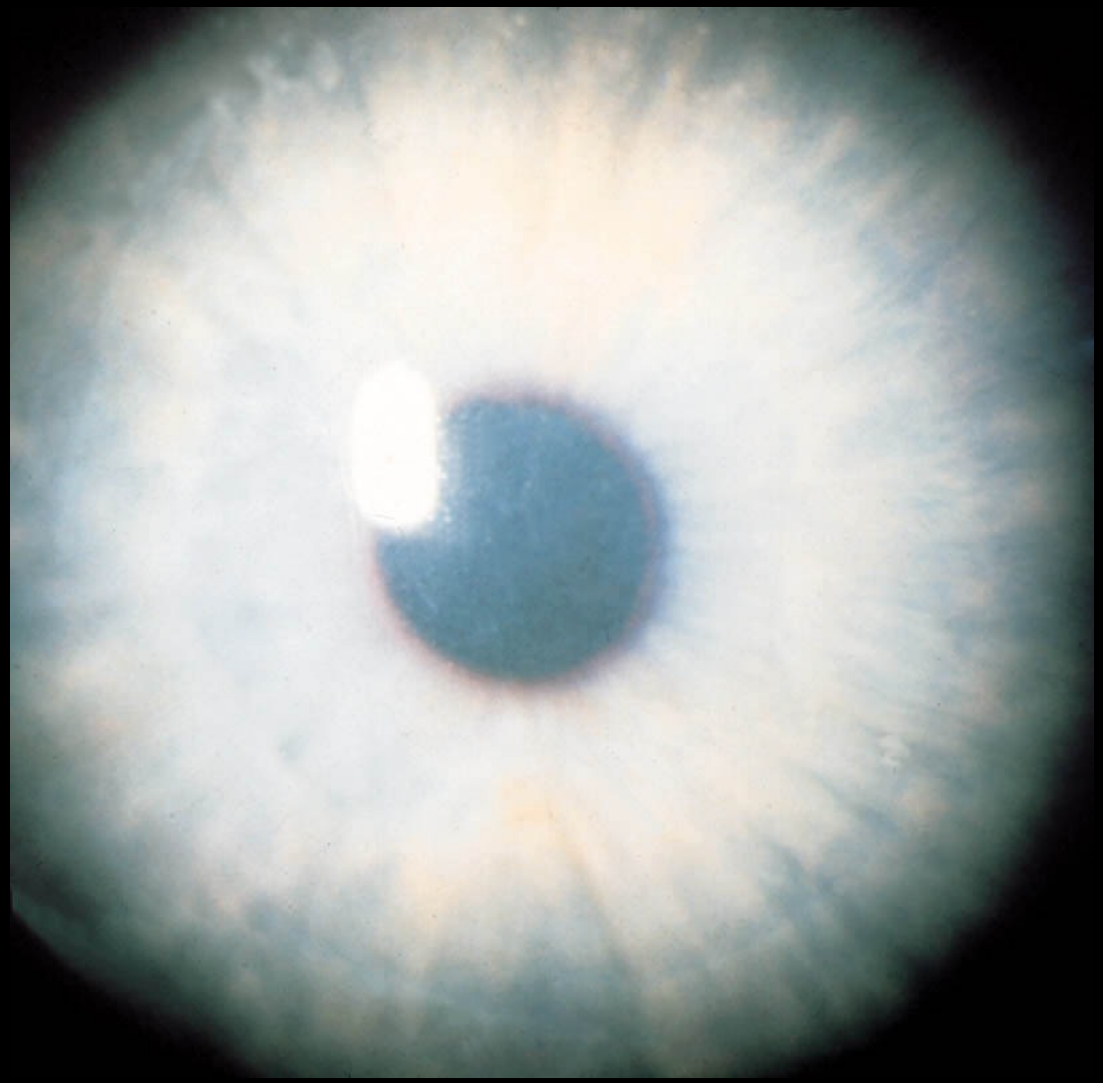
Scheie Syndrome



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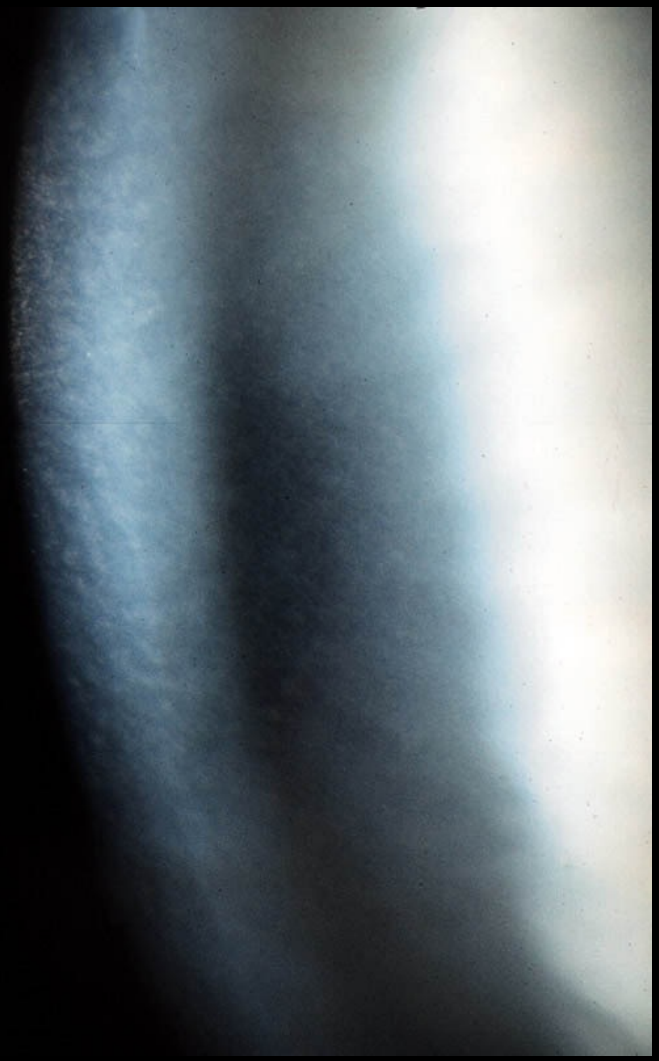
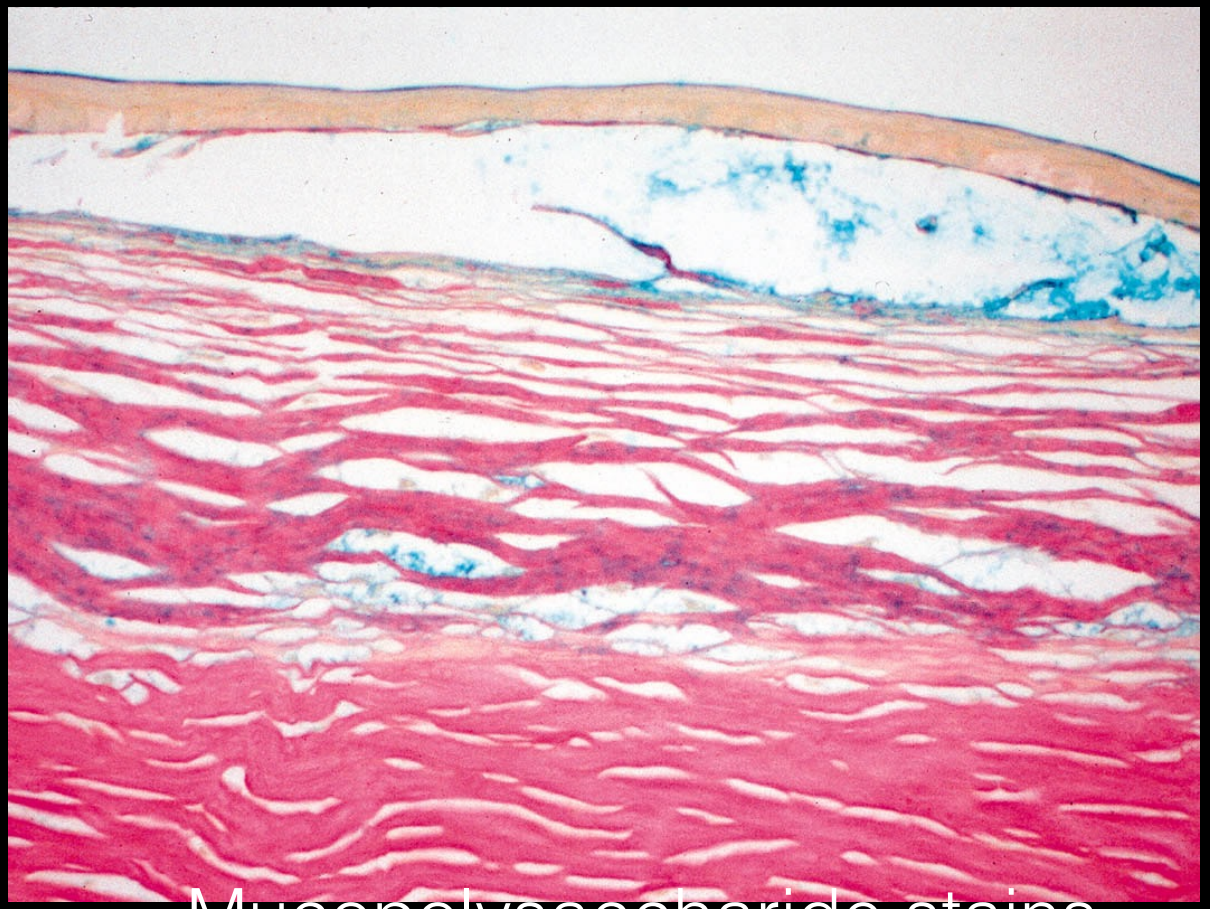
Scheie Syndrome





Mucopolysaccharide stains blue with an alcian blue stain

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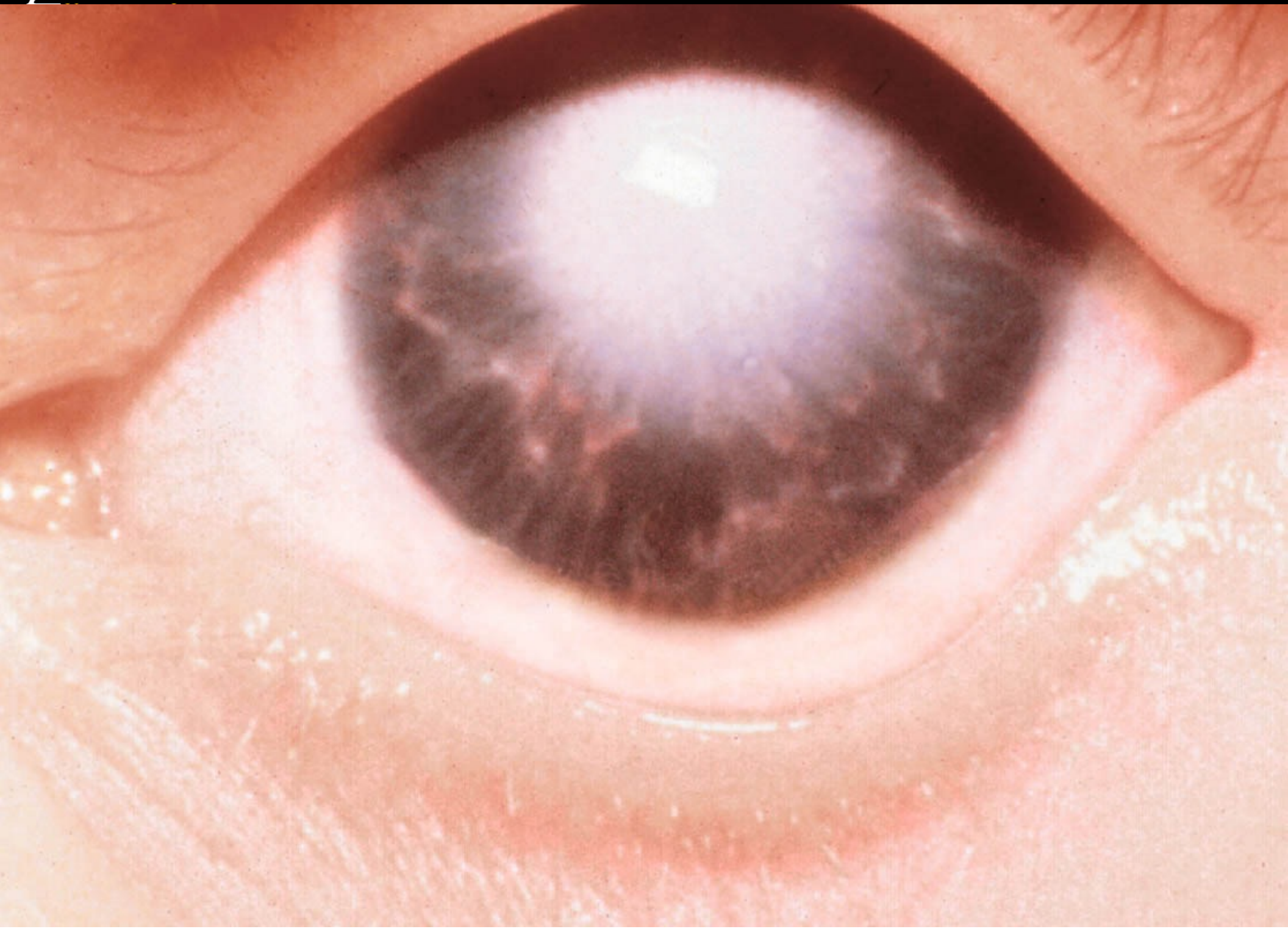
Peters Anomaly

- Posterior corneal endothelial defect
- Central stromal opacity
- May have adherent iris strands to edge of endothelial defect.
- Cornea may be vascularized
- Severe cases may have lens adherent to cornea (Peters type 2)
- Bilateral cases may also have other congenital abnormalities including cardiac



Peters Anomaly

- Often very poor visual outcome
- Pediatric corneal transplants usually end in graft failure
- Tremendous effort needed if infant PK undertaken
- Bilateral Peters requires surgery in at least one eye
- Unilateral Peters may benefit from PK after age 1

Congenital Hereditary Endothelial Dystrophy

- Uncommon (100's of cases only)
- Dominant or Recessive (2 different loci on Chromosome 20)
- Onset in infancy or at birth
- Endothelial cells abnormal, no guttata
- Diffuse corneal edema
- Normal IOP and corneal diameters
- Normal Anterior segment
- Corneal clouding usually less severe as child grows
- PK can be delayed

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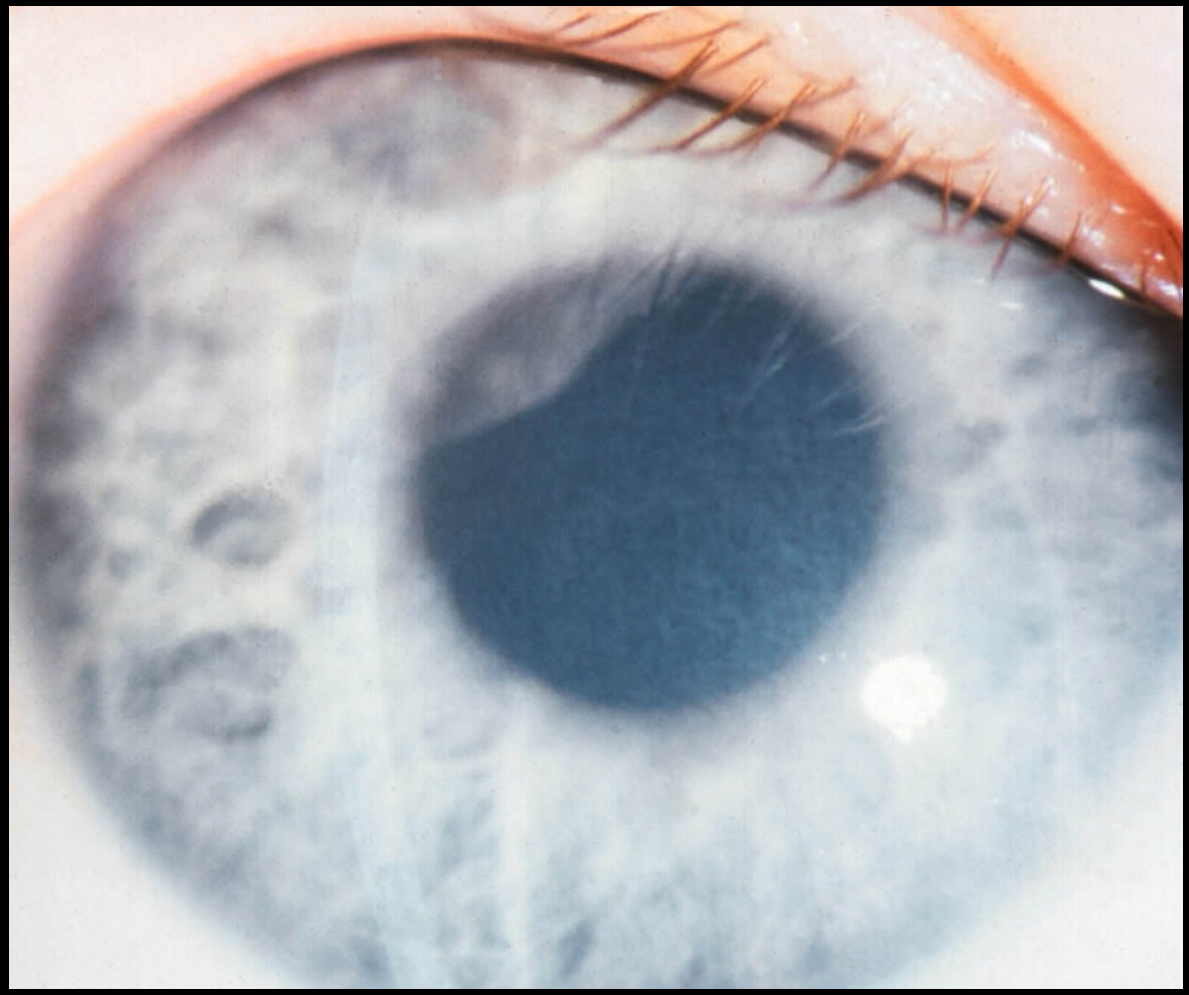
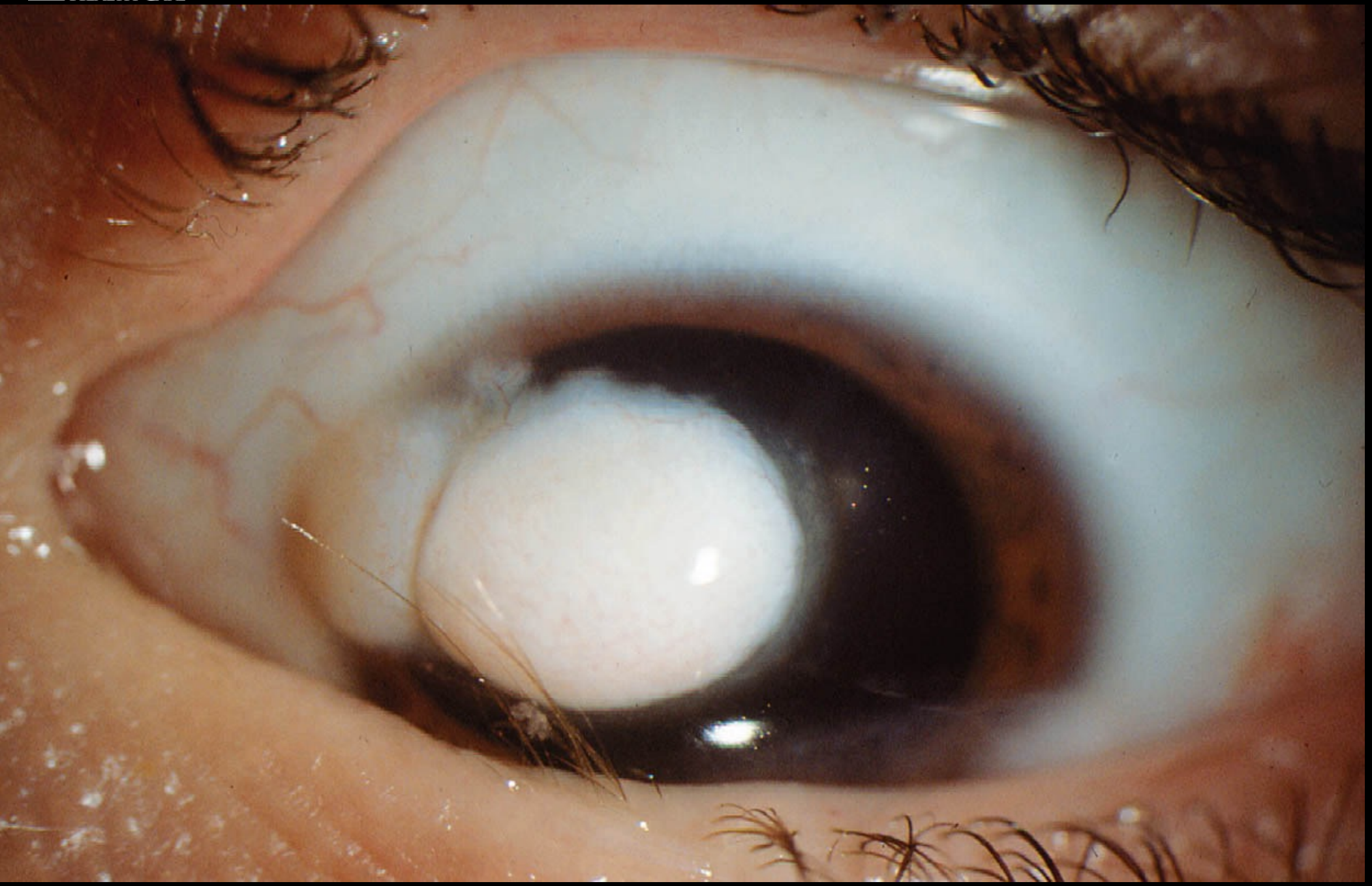
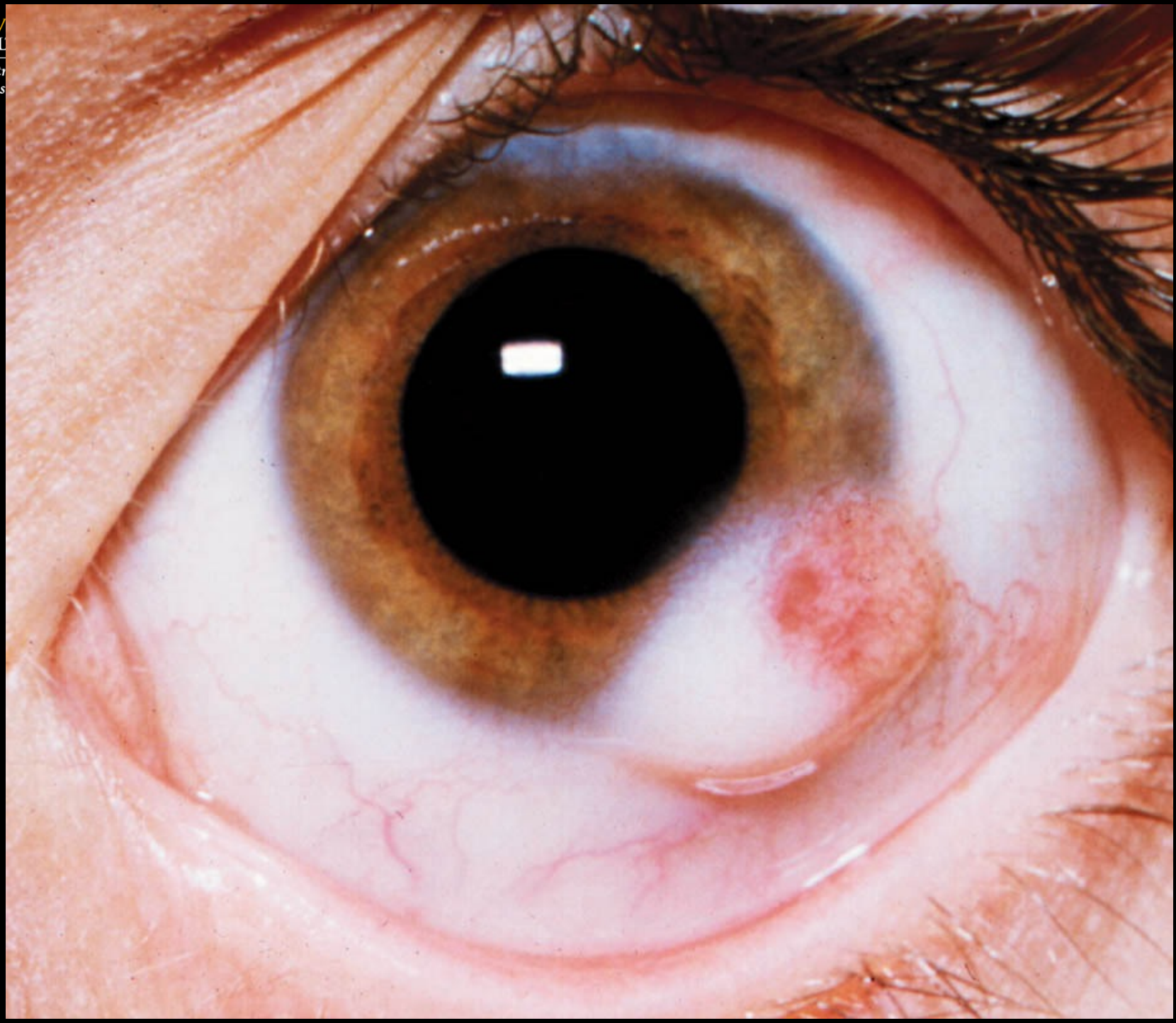
CHED



Corneal Dermoid

- Hamartoma
- Fibrous and fatty tissue with keratinizing epithelium
- May contain hair and glands
- Usually cover limbus and are partial thickness, usually well tolerated
- May obscure visual axis or cause astigmatism leading to ambylopia
- Associations: Goldenhar syndrome





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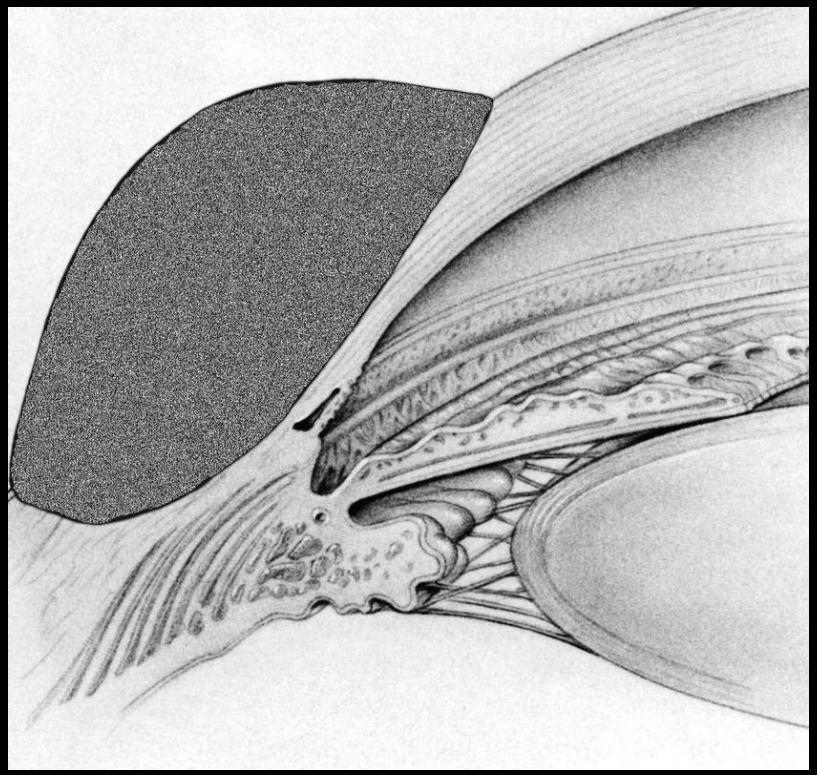
Corneal Dermoid

- Lamellar excision may be necessary
- Avoid anterior chamber penetration
- Excision often leaves child with astigmatism and scar
- May need corneal or scleral patch graft primarily



Cystinosis

- Increased intracellular cystine
- Leads to failure to thrive, kidney failure and corneal deposits as early as the first year of life
- Photophobia may be severe
- Oral cysteamine for the systemic deposits
- Topical cysteamine (q2h)- currently not available pending FDA approval

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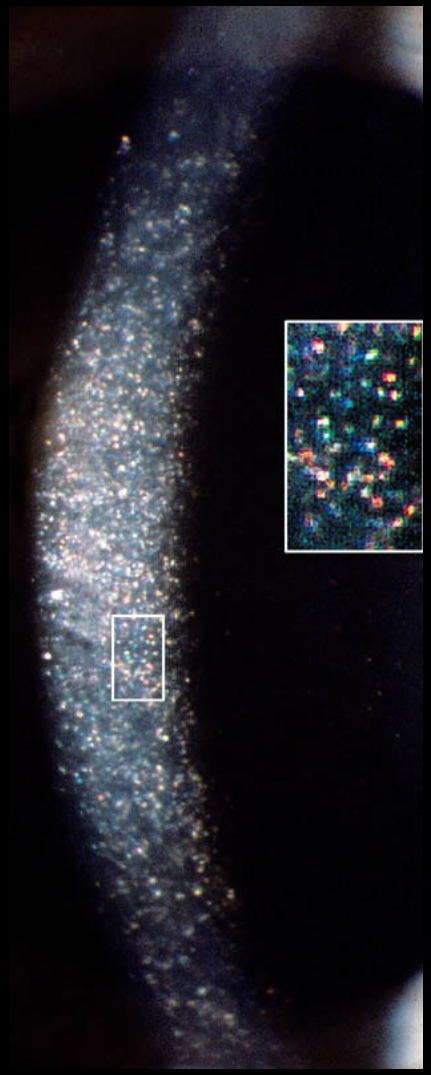
Cystinosis



- Crystals are anterior stromal initially
- Polychromatic
- Needle shaped to rectangular

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Wilson's Disease

- Hepatolenticular degeneration
- Autosomal recessive
- Excess copper depostion in liver, kidney, basal ganglia
- Cirrhosis, kidney failure, movement disorder
- Kaiser-Fleischer ring
  - Copper depostion in Decemet's membrane
  - Initially at 12 and 6 o'clock
  - Resolves with systemic treatment
  - Late finding but occurs in nearly every case of CNS dysfunction
- Sunflower cataract: copper deposition in lens capsule
- Laboratory testing can detect condition earlier
  - Elevated serum and urinary copper
  - Low serum ceruloplasmin
- D-penicillamine, trien, or zinc acetate

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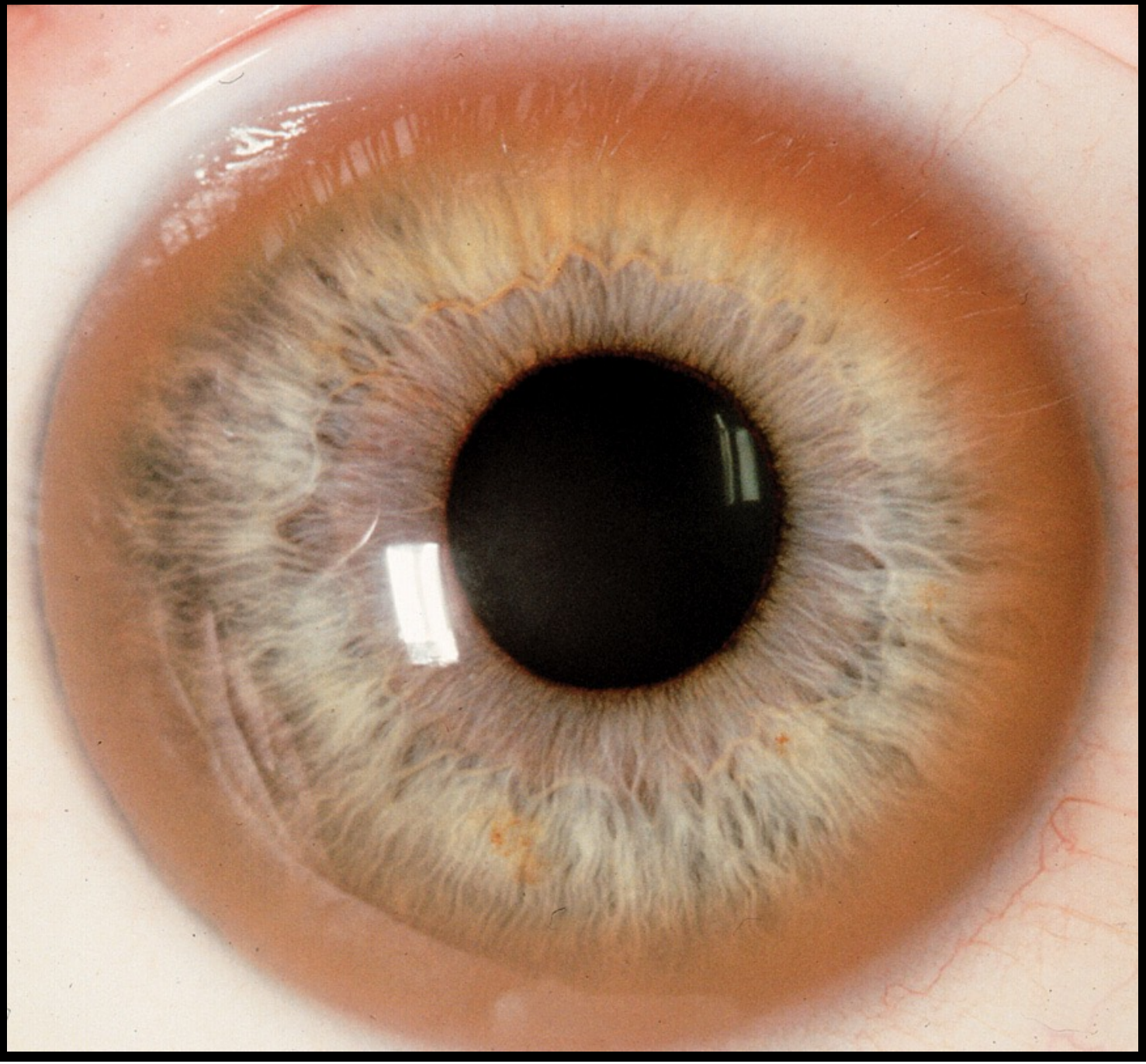

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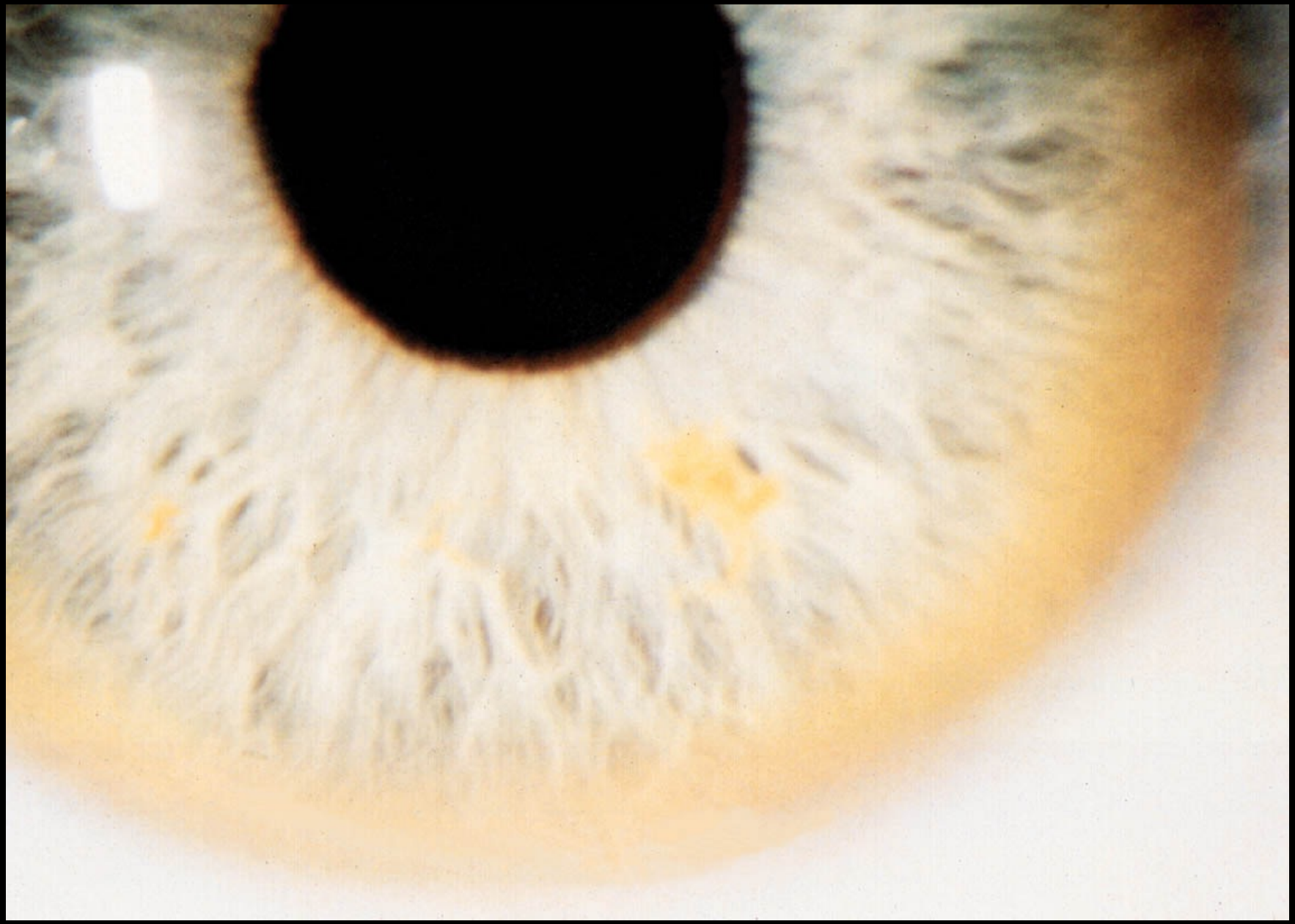

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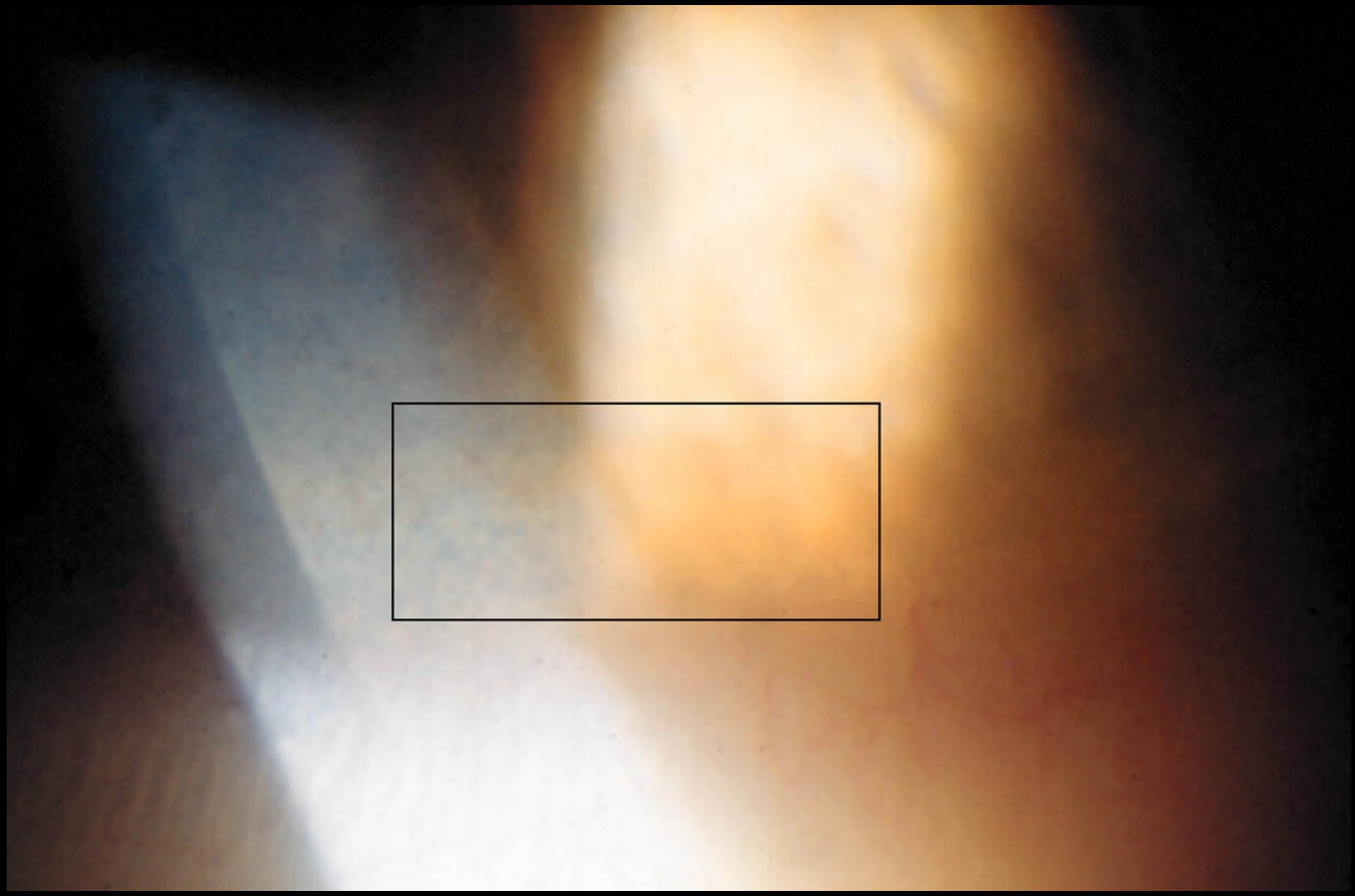

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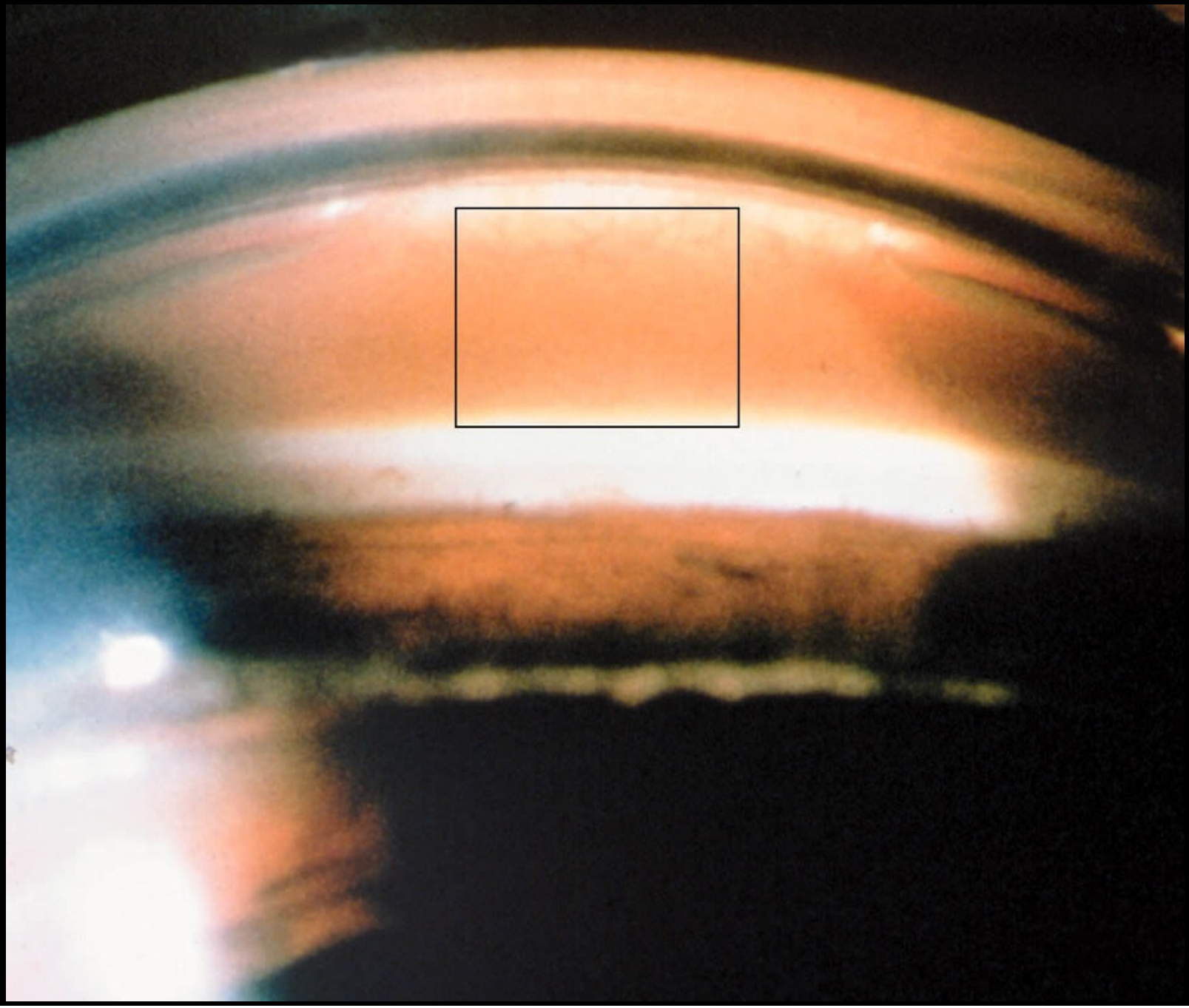

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Anterior Segment Dysgenesis

- AKA: mesenchymal dysgenesis, anterior chamber clevage syndrome, mesectodermal dysgenesis
- Peripheral
  - Axenfeld-Reiger syndrome
- Central
  - Peters anomaly

Axenfeld-Rieger

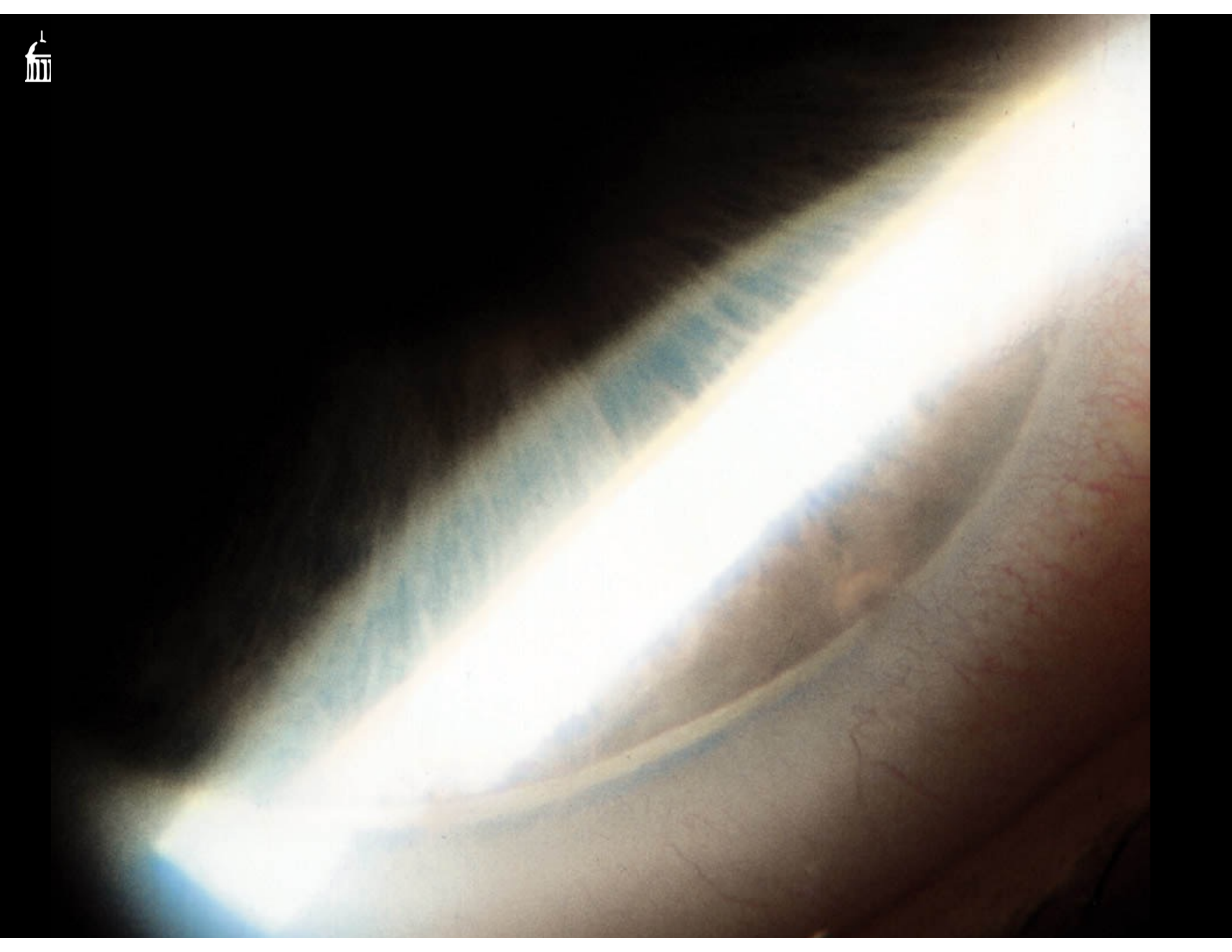
- Arrest of anterior segment development late in gestation
- Glaucoma from compact, ineffective trabecular tissue
- Autosomal Dominant
  - Chromosome 4q (REIG1 or called PITX2 gene)
    - PITX2 gene is a paired homeobox gene controlling expression of other genes
  - Chromosome 13q
  - Chromosome 6p (FKHL7)
    - some cases of Axenfeld anomaly and Rieger anomaly without systemic abnormalities

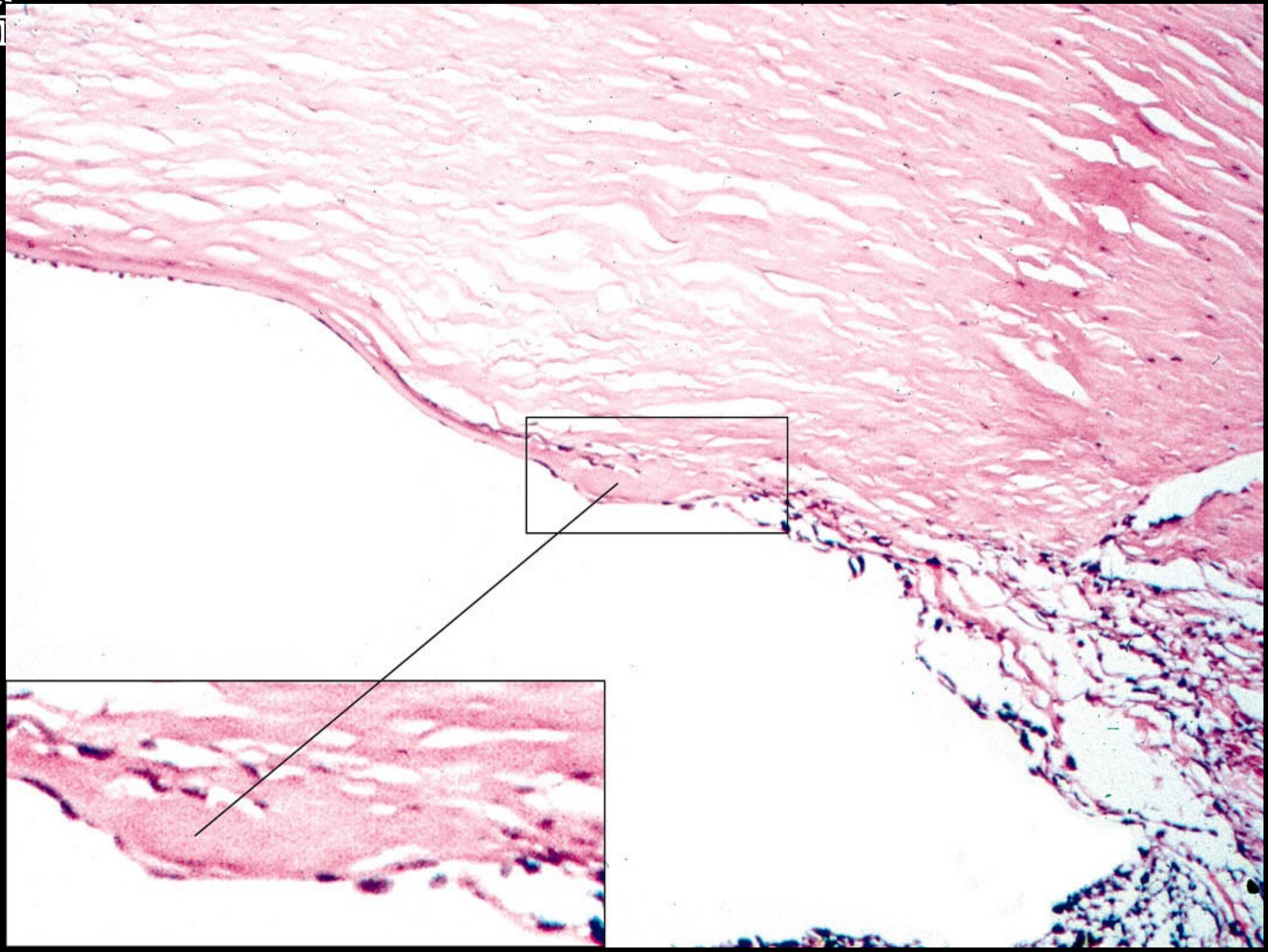
Axenfeld-Rieger

- Bilateral
- Glaucoma in 50%- related to level of iris insertion, higher = greater risk
- Posterior Embryotoxin:
  - glassy, white line on corneal endothelium = prominent anterior Schwalbe's line.
  - Seen in 15% of normals
  - By itself not associated with glaucoma.
  - Not necessary for diagnosis but seen in nearly all.

Posterior Embryotoxin

- Other associations
  - Megalocornea
  - Alagille syndrome (Arteriohepatic dysplasia)





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Axenfeld-Rieger

- Axenfeld anomaly = Post. Embryotoxin and iris processes
- Axenfeld syndrome = Axenfeld anomaly + glaucoma
- Rieger anomaly = Axenfeld anomaly + iris hypoplasia, polycoria or correctopia
- Rieger syndrome = Rieger anomaly + systemic abnormalities

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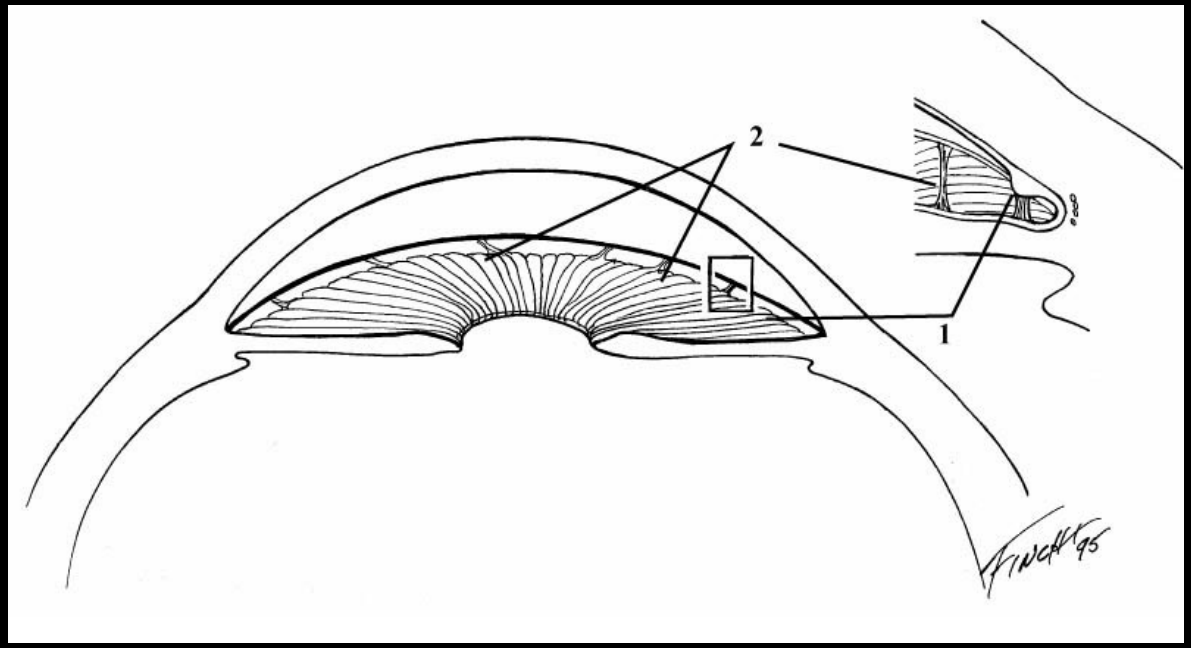
Axenfeld anomaly

- Posterior embryotoxin + iris processes
- Iridocorneal angle: prominent iris processes. Iris may insert high in the angle.



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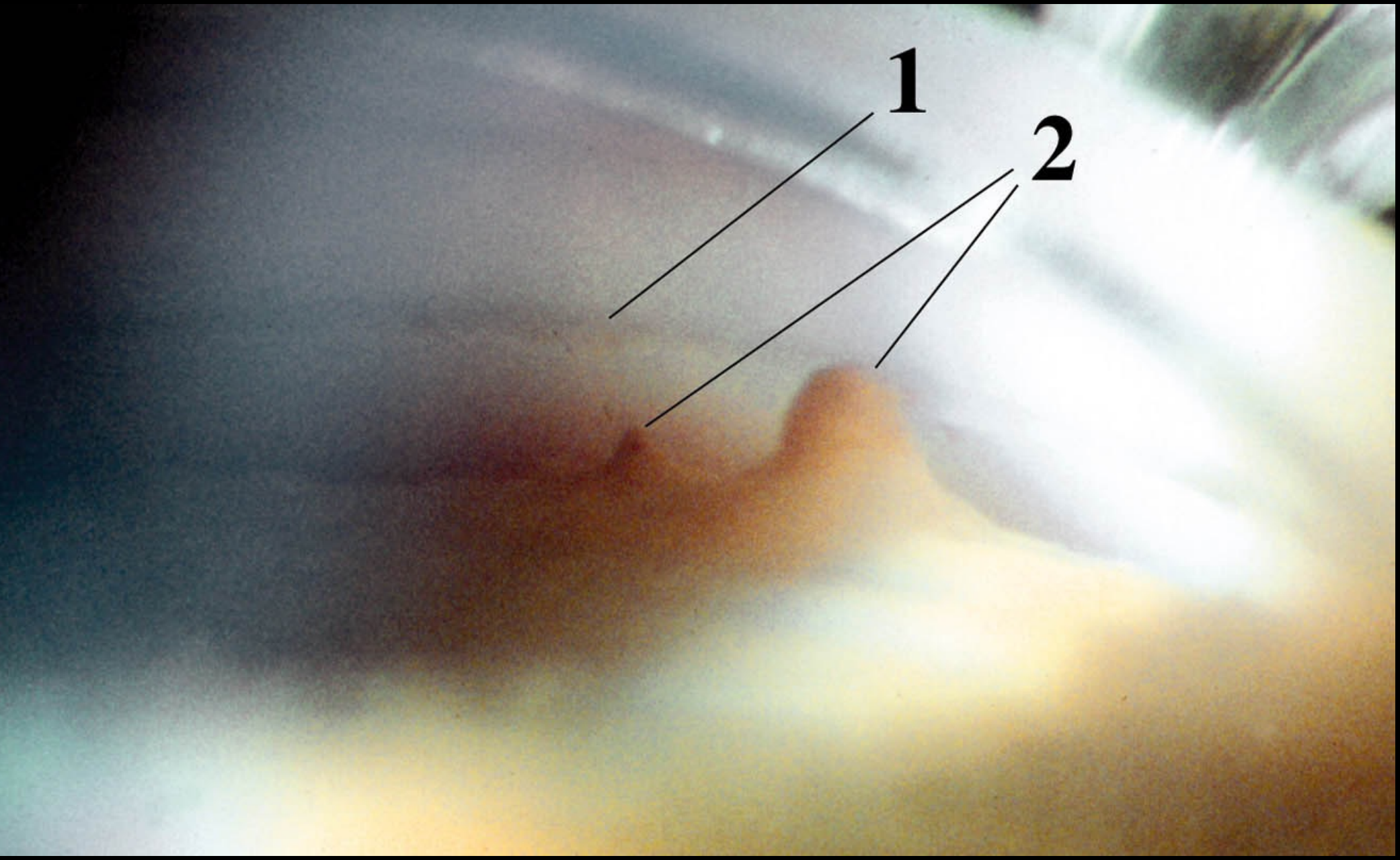

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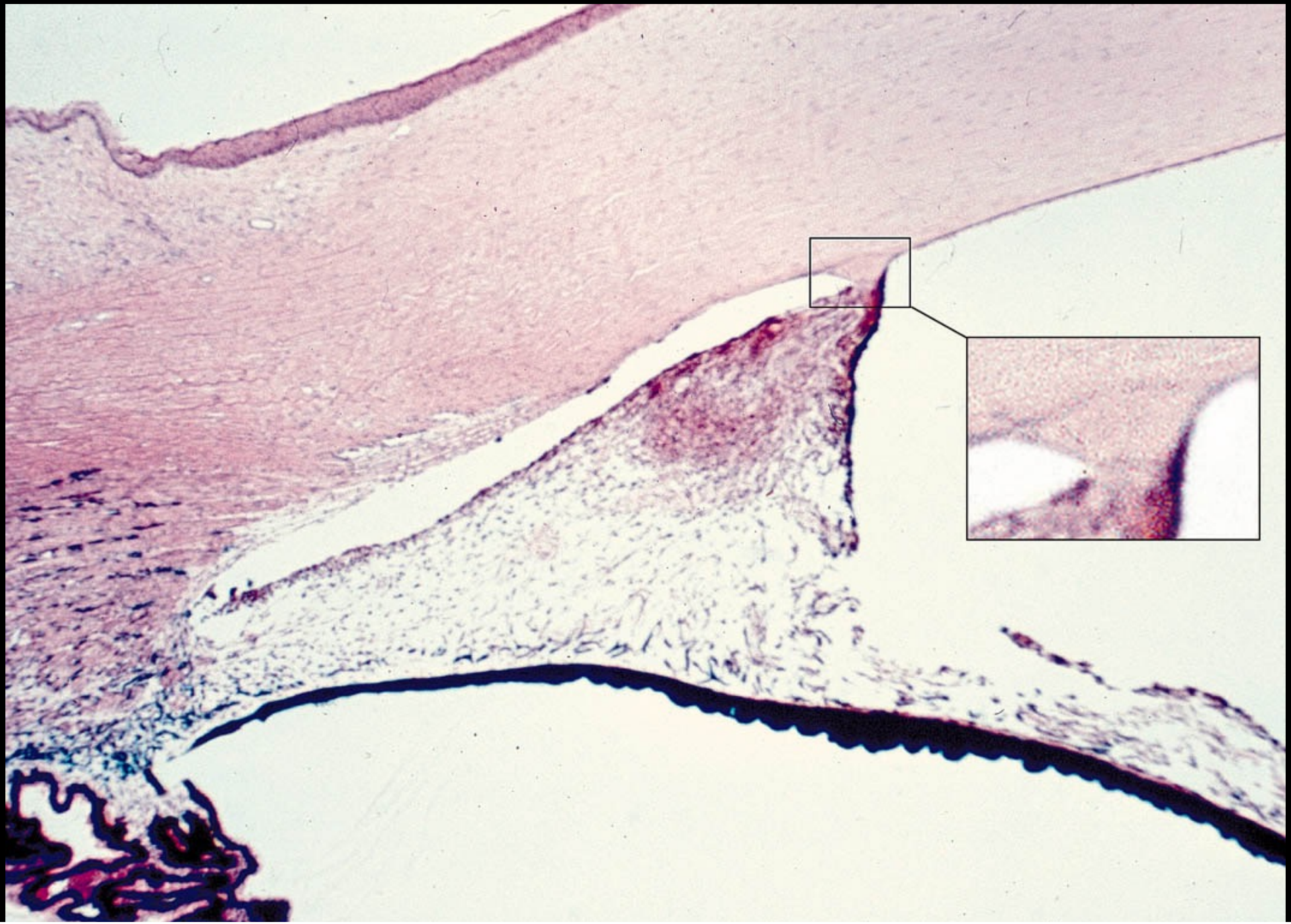
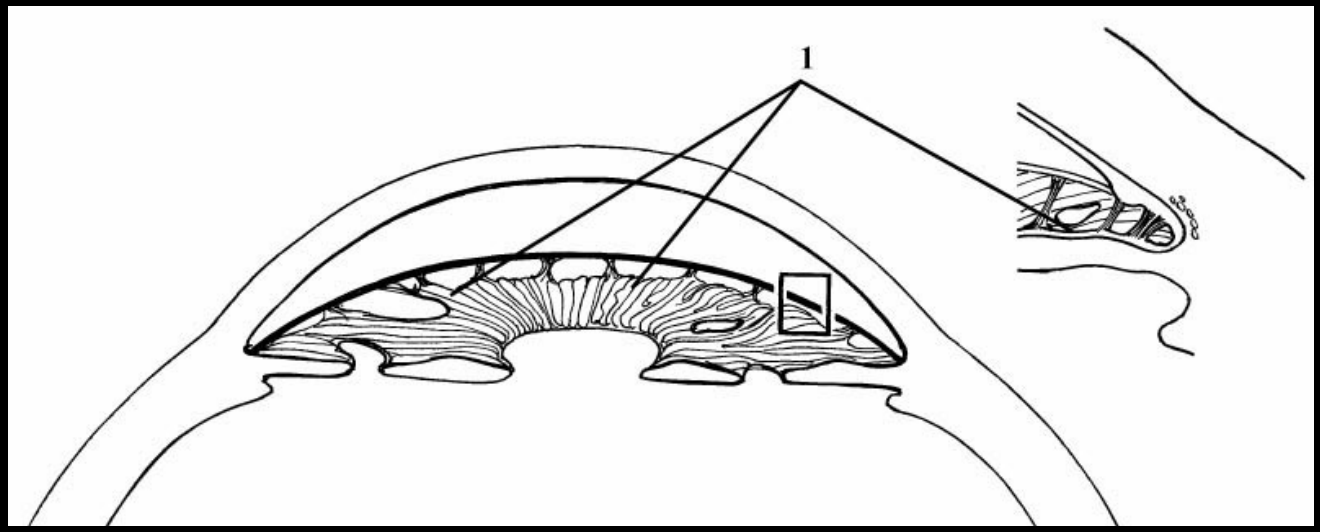
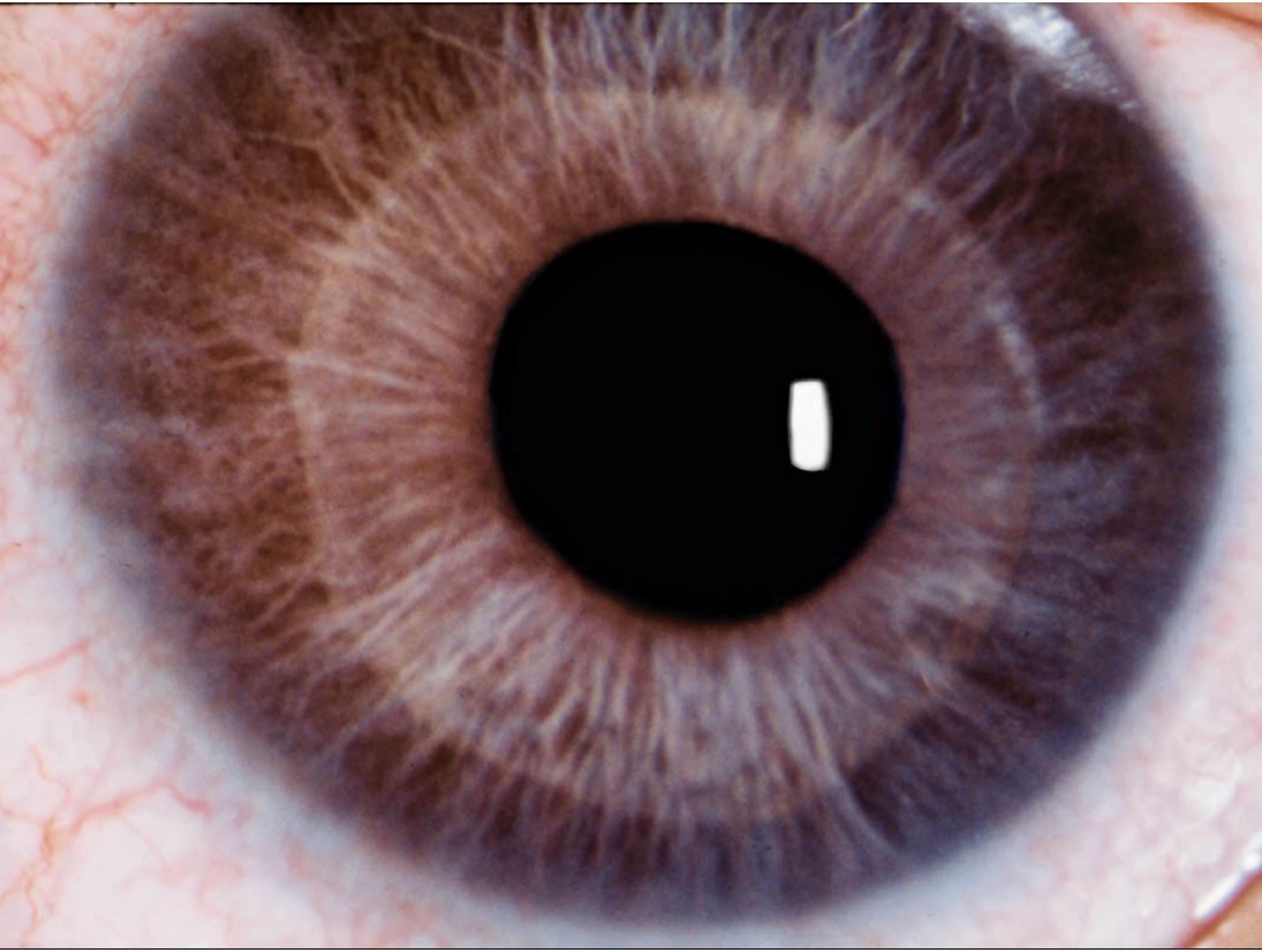


Axenfeld-Rieger

- Rieger anomaly
  - posterior embryotoxin + iris processes + iris hypoplasia, corectopia, or polycoria
  - Iris is thin and hypoplastic.
  - Sphincter stands out as a ring, corectopia, polycoria, changes are usually static.





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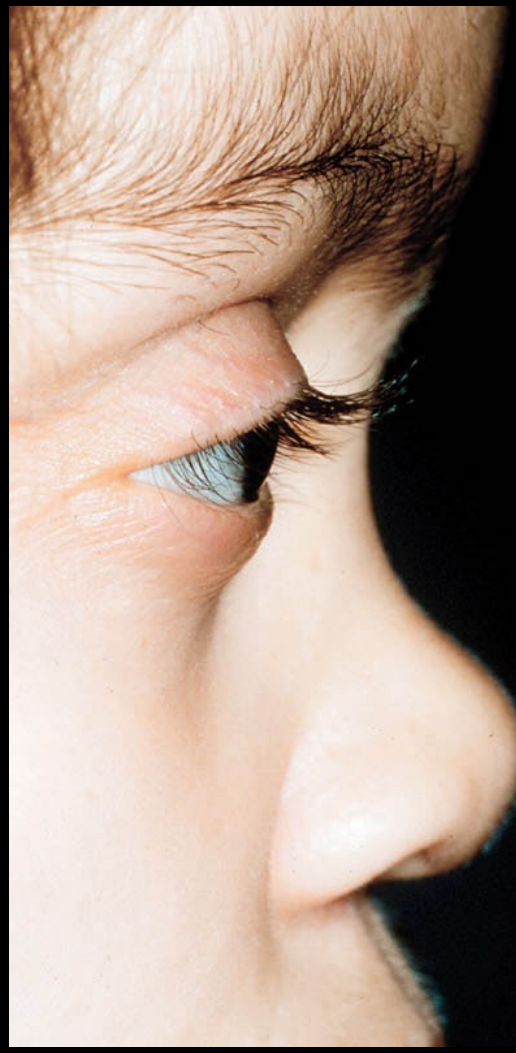
Axenfeld-Rieger

- Rieger Syndrome
- Non-ocular findings
  - mid-face flattening
  - maxillary hypoplasia
  - hypertelorism, telecanthus
  - broad & flat nasal bridge
  - hypodontia (too few)
  - microdontia
  - redundant periumbilical skin
  - hypospadias
  - growth hormone deficiency
  - empty sella



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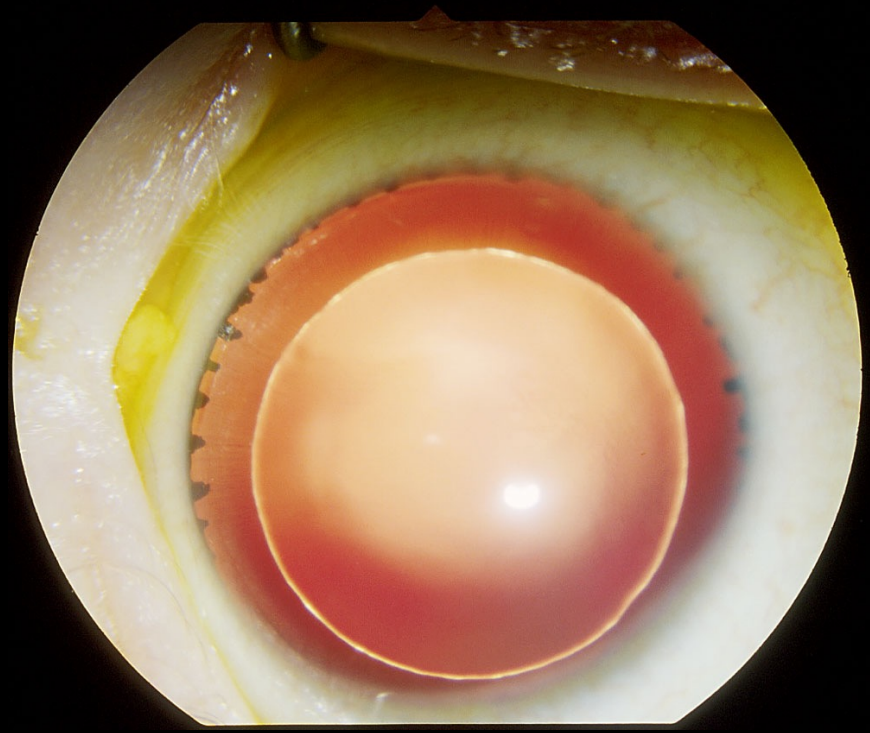
Aniridia

- Defect in PAX6 gene
- Panocular condition
  - Glaucoma 50-60%- secondary angle closure
  - Cataract
  - Foveal hypoplasia
    - Nystagmus,
    - poorer vision
  - Corneal pannus



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Aniridia

- Wilms tumor (WT1 gene)
- Aniridia (PAX6 gene)
- Genitourinary abnormalities
  - cryptorchidism, hypospadias, pseudohermaphroditism, renal abnormalities
- Mental Retardation

- FISH testing for deletion
- Regular Abdominal US for Wilm's tumor first 14 years of life

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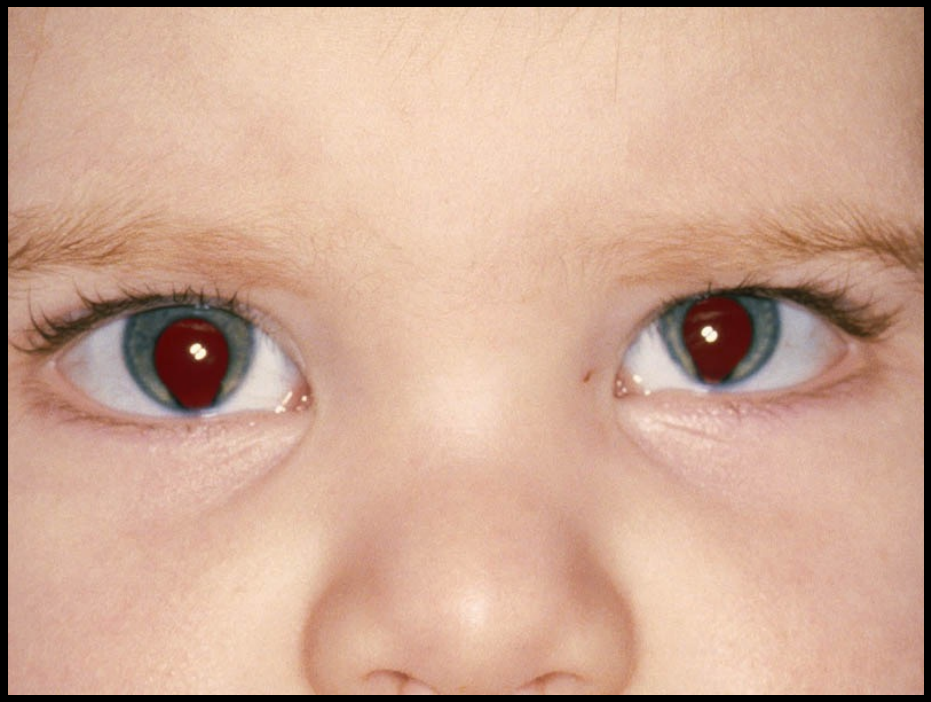
Iris Colobomas

- Inferior nasal quadrant = “typical”
- Failure of closure of embryonic fissure in week 5 of gestation
- May involve ciliary body, choroid, retina, optic nerve
- Associated with microphthalmia
- Autosomal dominant transmission most common
- May be associated with chromosomal abnormality if another organ system affected
- Look at parents may be very subtle



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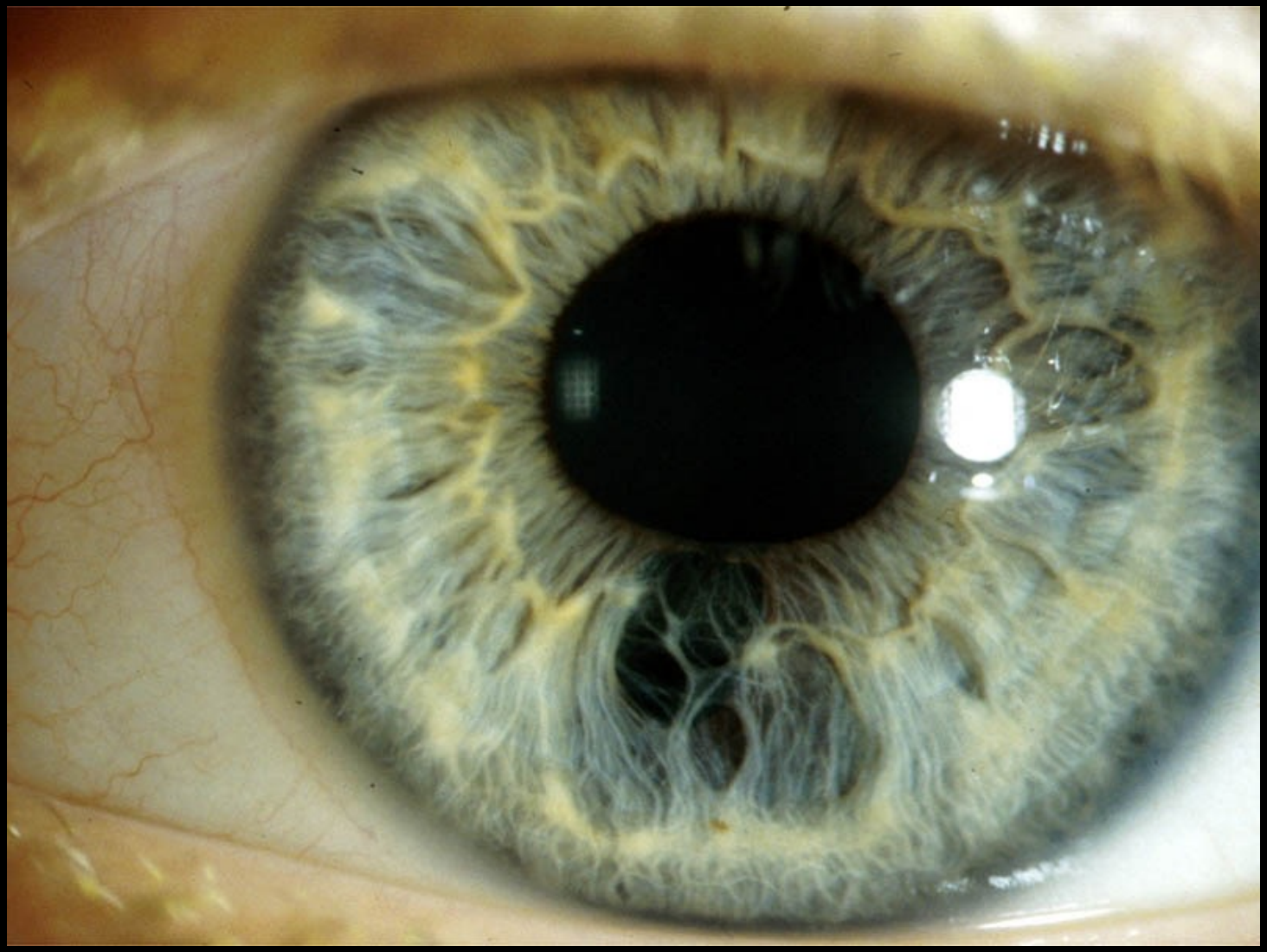
Iris Coloboma



Pigment Epithelial Cysts

- Most common in childhood
- Separation of pigment epithelial layers
- Ruptured cysts at pupil margin: flocculi
- Excision or rupture with Yag or Argon laser- if affect vision

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Iris Stromal Cysts

- Uncommon
- Surface ectoderm trapped in iris tissue
- Cyst lined with epithelial like tissue that can cover anterior segment
- Cryo with needling
- En Bloc excision
- Proceed with extreme caution

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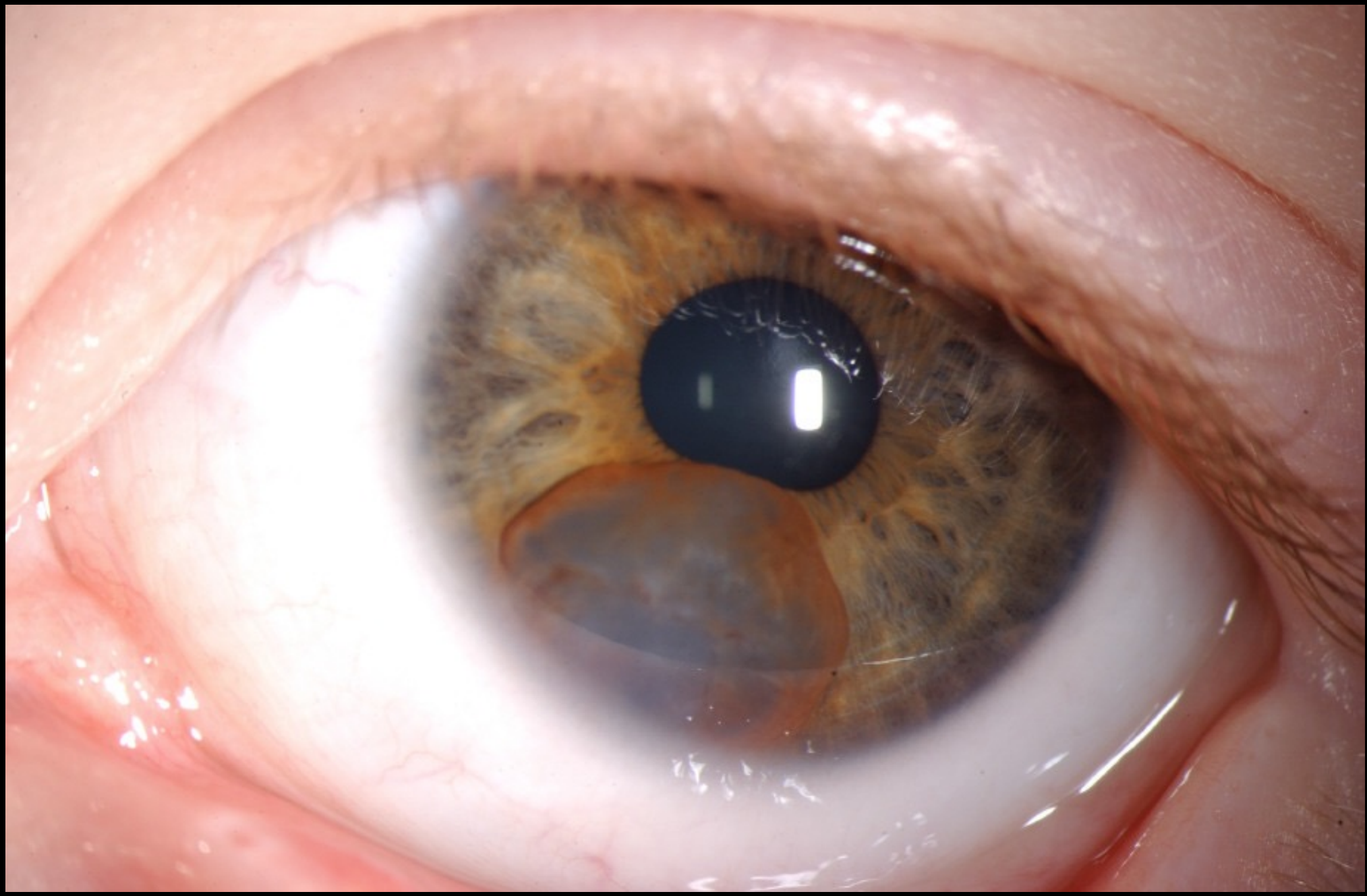

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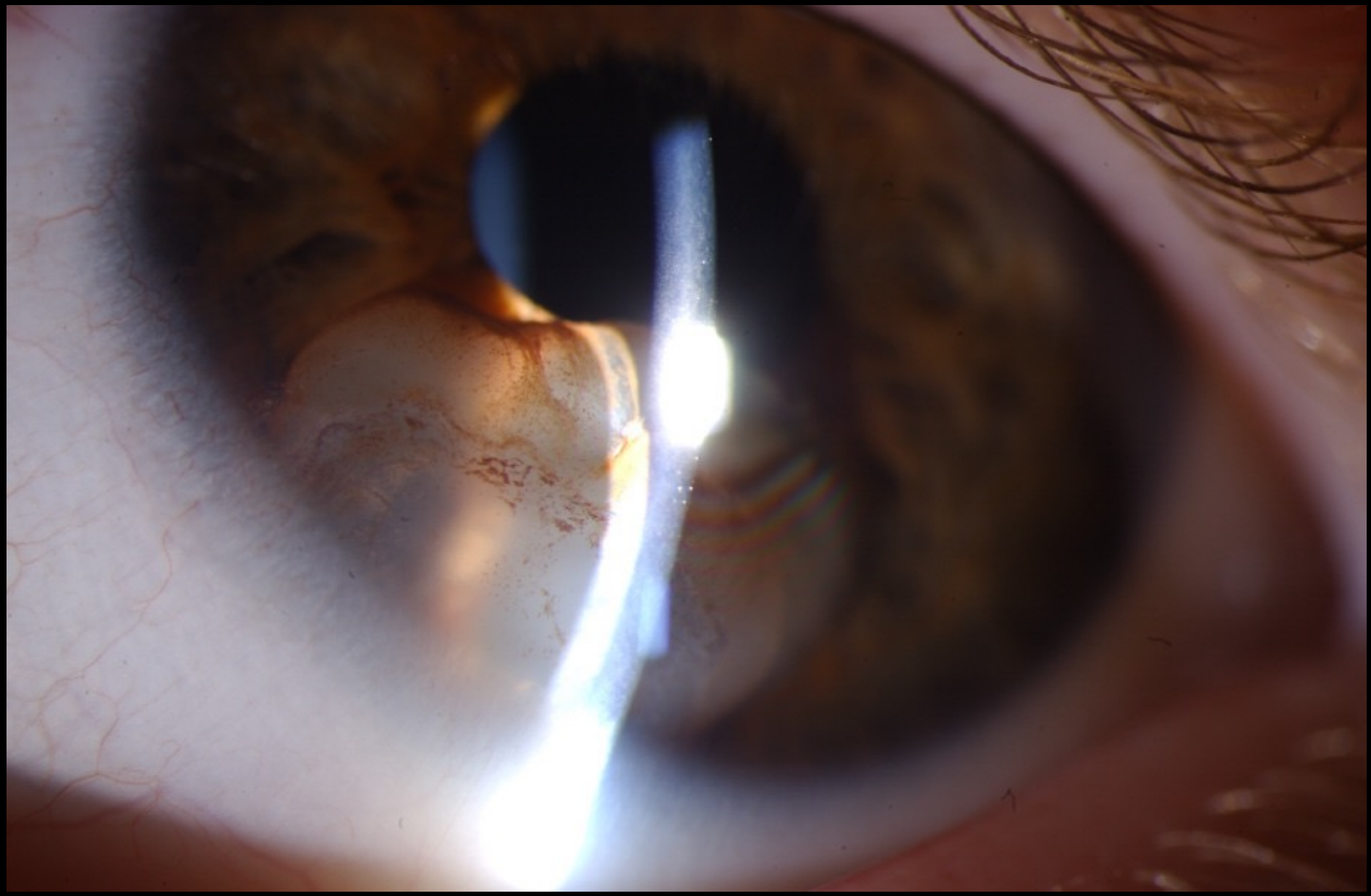

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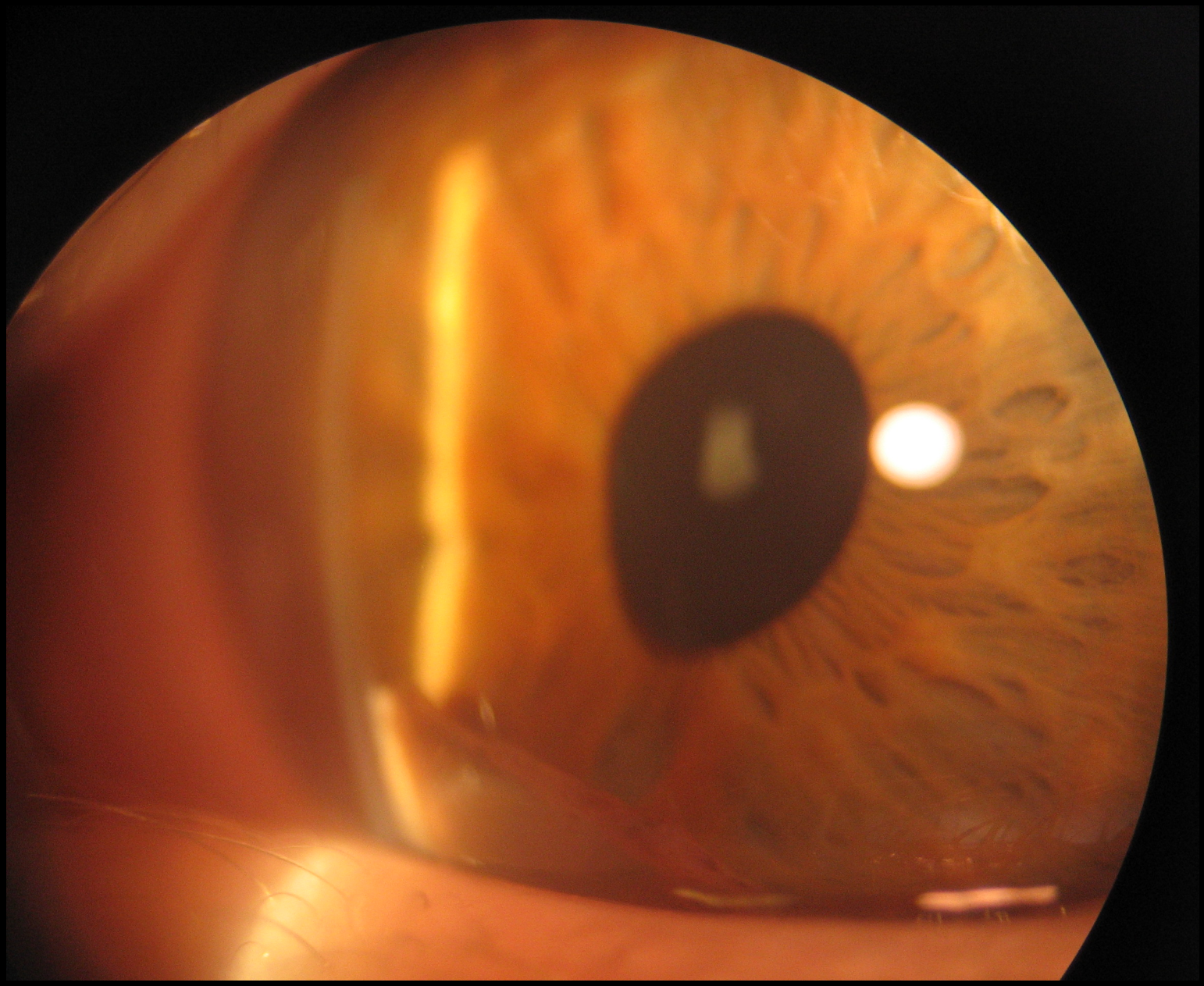

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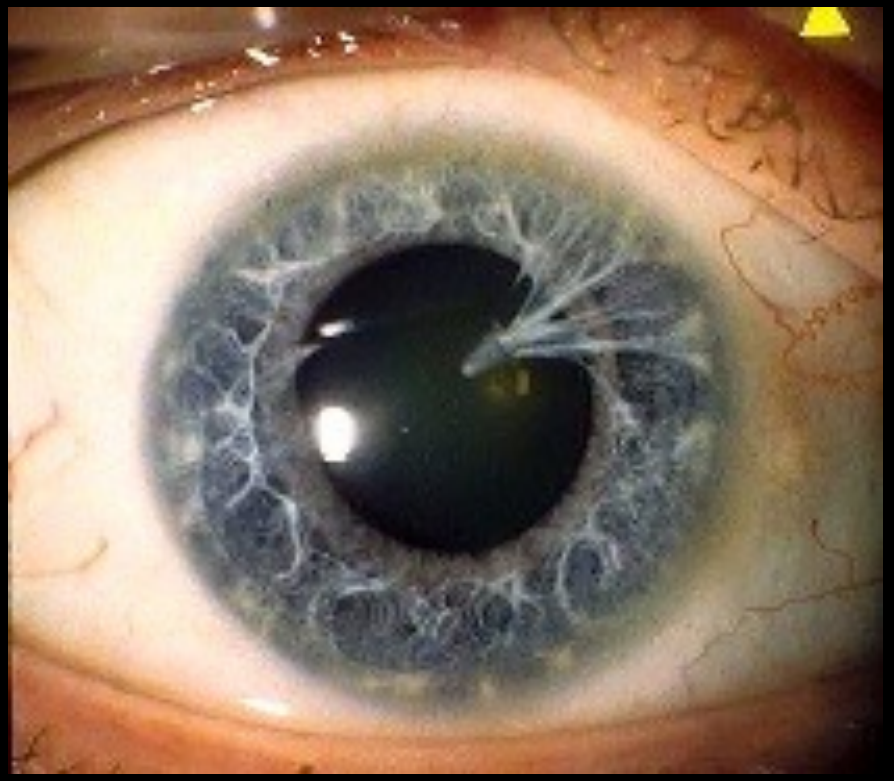
Persistent Pupillary Membrane

- Most common iris developmental abnormality
- May cause very poorly opening pupil
- May obstruct visual axis
- May adhere to lens capsule and have small associated cataract
- Usually does not require intervention



Lens Abnormalities

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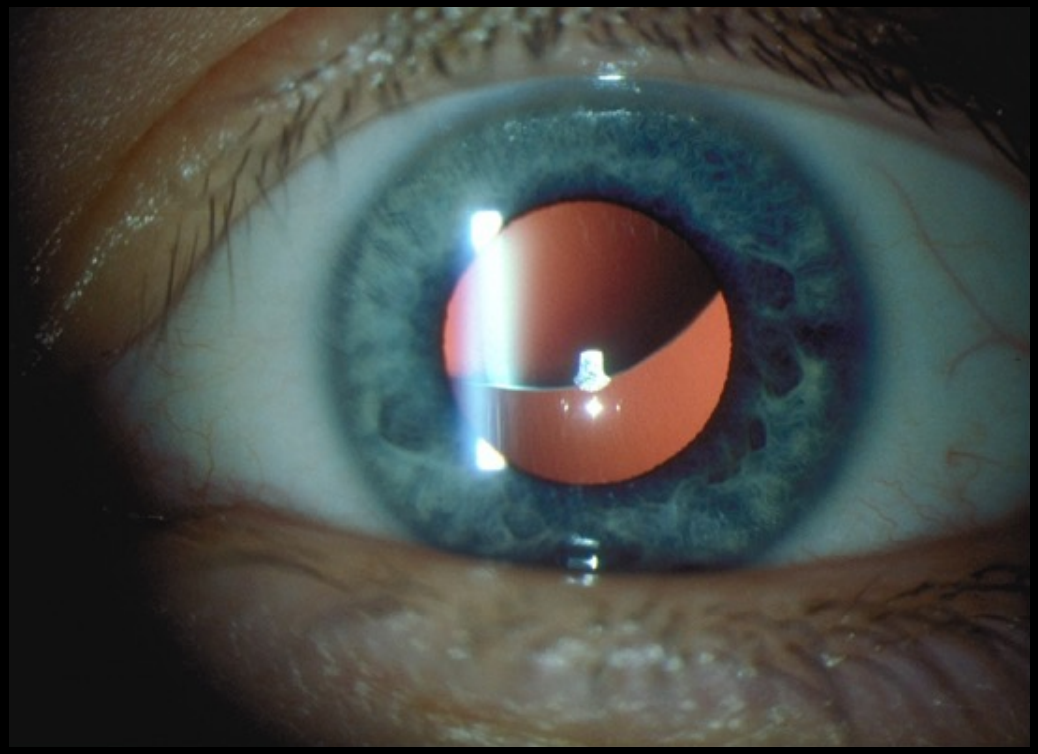
Lens Subluxation/Dislocation

- Primary ocular
  - Trauma (most common)
  - Simple ectopia lentis
  - Ectoptia lentis et pupillae
  - Buphthalmos
  - Exfoliation syndrome
  - Aniridia
- Systemic
  - Marfan syndrome
  - Weill-Marchesani syndrome
  - Homocystinuria
  - Hyperlysemia
  - Sulfite oxidase deficency
  - Ehlers-Danlos syndrome I
  - Syphilis



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Pediatric Cataracts

- 1/250 newborns
- Inherited types: usually Autosomal dominant
- Genes controlling cataract formation linked to chromosome 1,2,16,17
- Chromosomal abnormalities: trisomy 13,18,21
- History and morphology important in understanding etiology

Pediatric Cataracts

- Consider work-up if…
  - bilateral nuclear or cortical cataracts without a family history
  - other organ systems involved
  - certain morphological types
  - associated with other affected systems
- Pediatric Genetics evaluation may helpful
- Use proper imaging if fundus not visible!!

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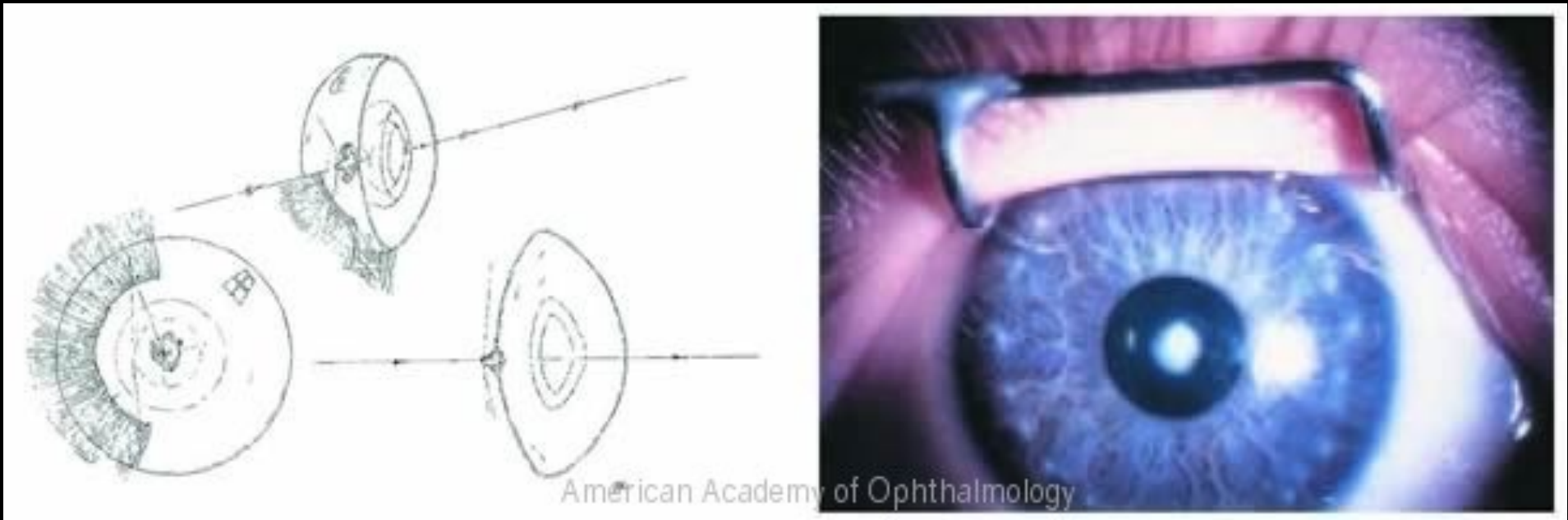
Polar Cataracts

- Developmental abnormality of lens vesicle
- Anterior more common
- Most anterior cataracts affect vision less
  - Usually > 3mm in diameter
- Polar cataracts (anterior or posterior) often include the capsule



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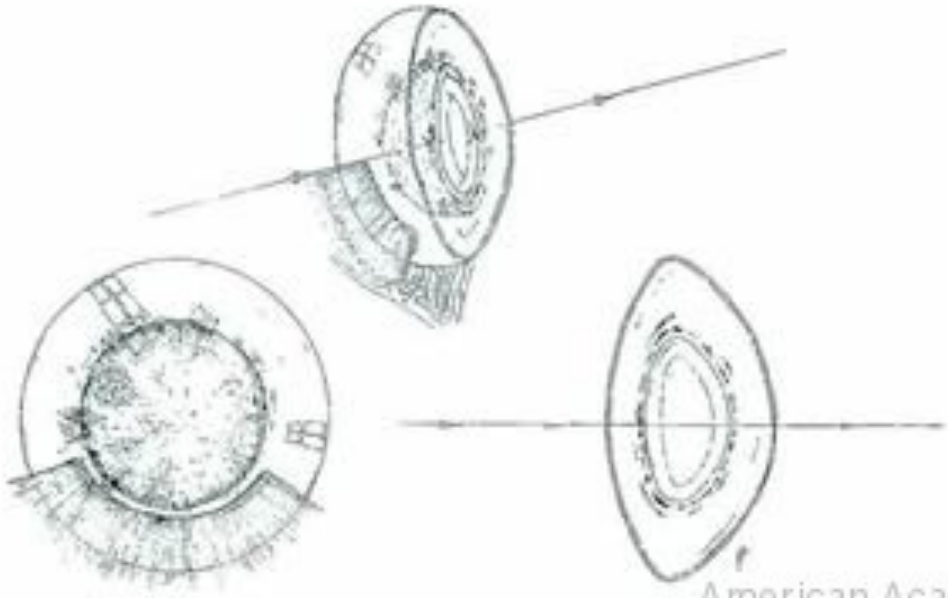
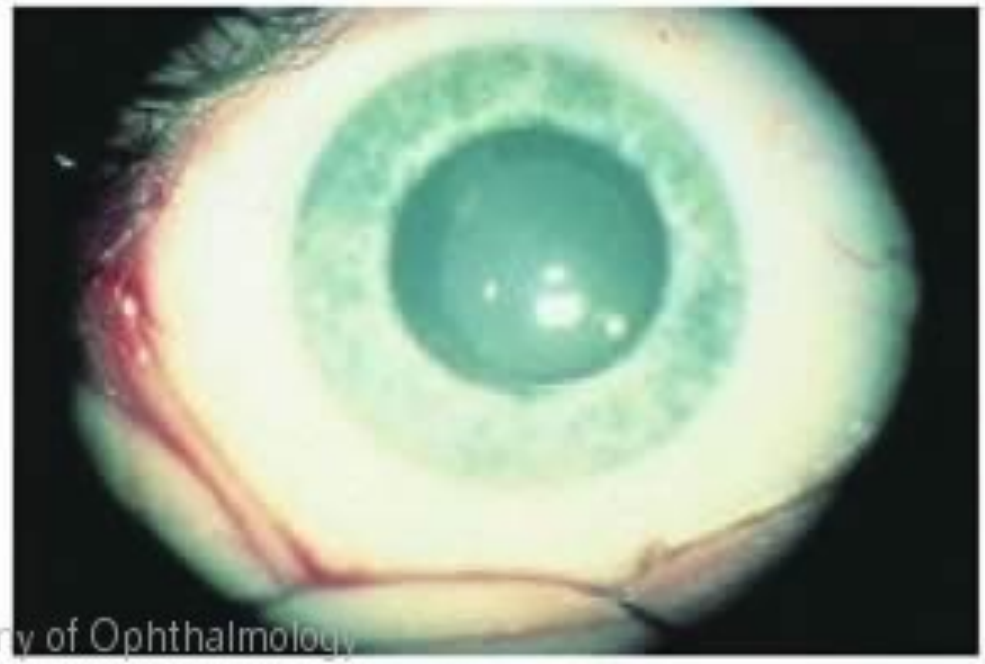
Lamellar cataracts

- Opacification peripheral to the Y sutures (aka. Zonular)
- Often inherited, progressive, bilateral
- Association: Neonatal tetany, hypoparathyroidism
- Work up: serum calcium, phosphorus and parathormone levels





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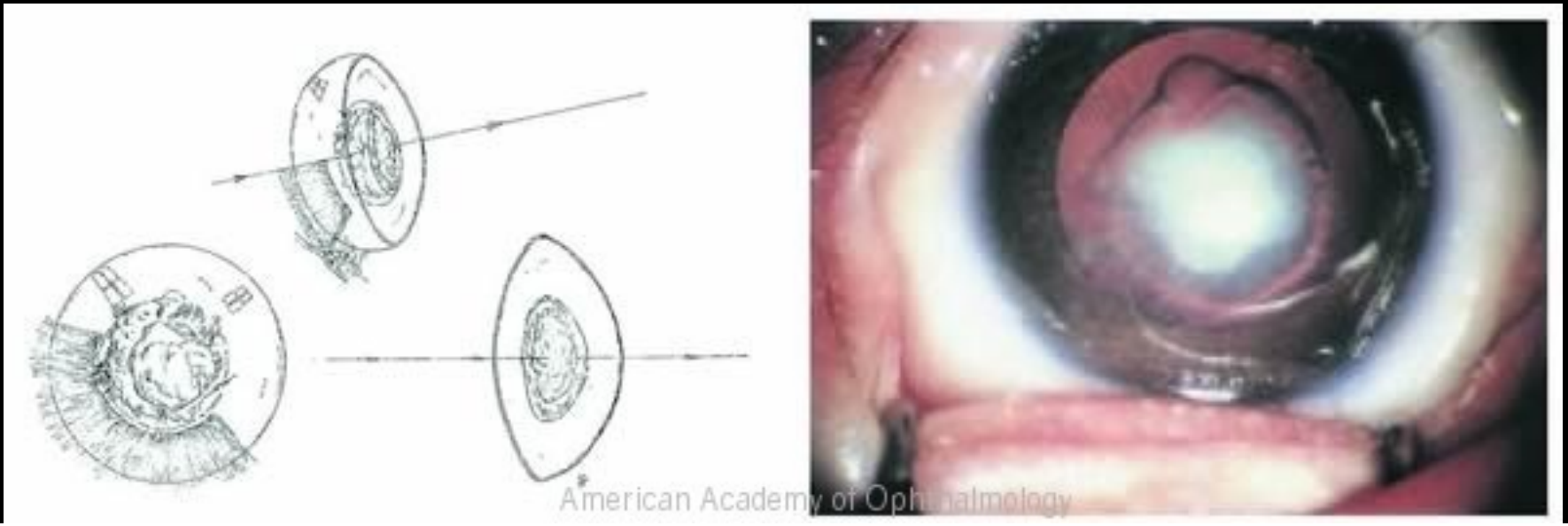
Nuclear Cataract

- More dense involving fetal nucleus
- Often inherited, autosomal dominant
- Microphthalmia more common
- Associations: Rubella, Varicella
- Work up: TORCH titer or neonatal and maternal rubella IgM antibody, ELISA for varicella serum antibody



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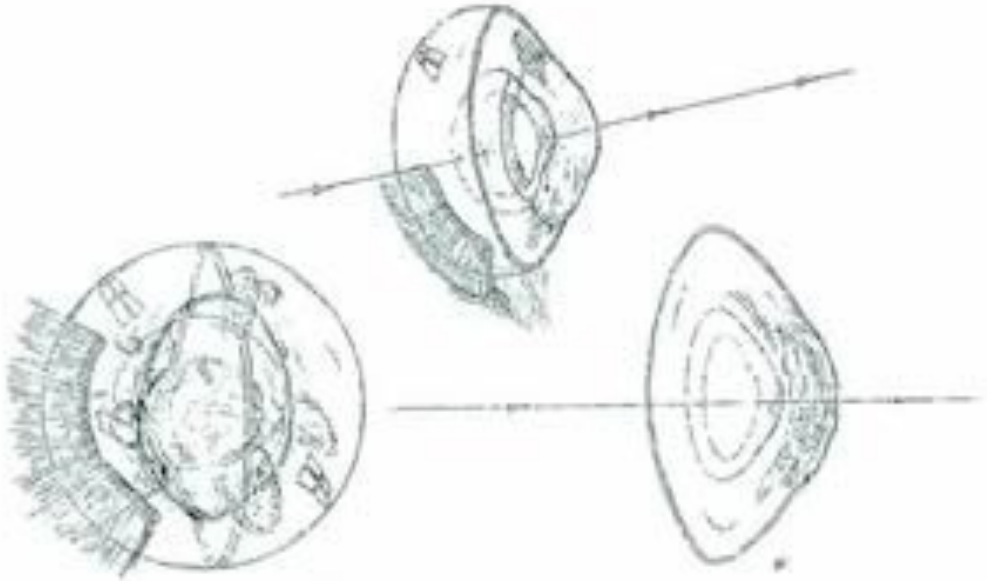
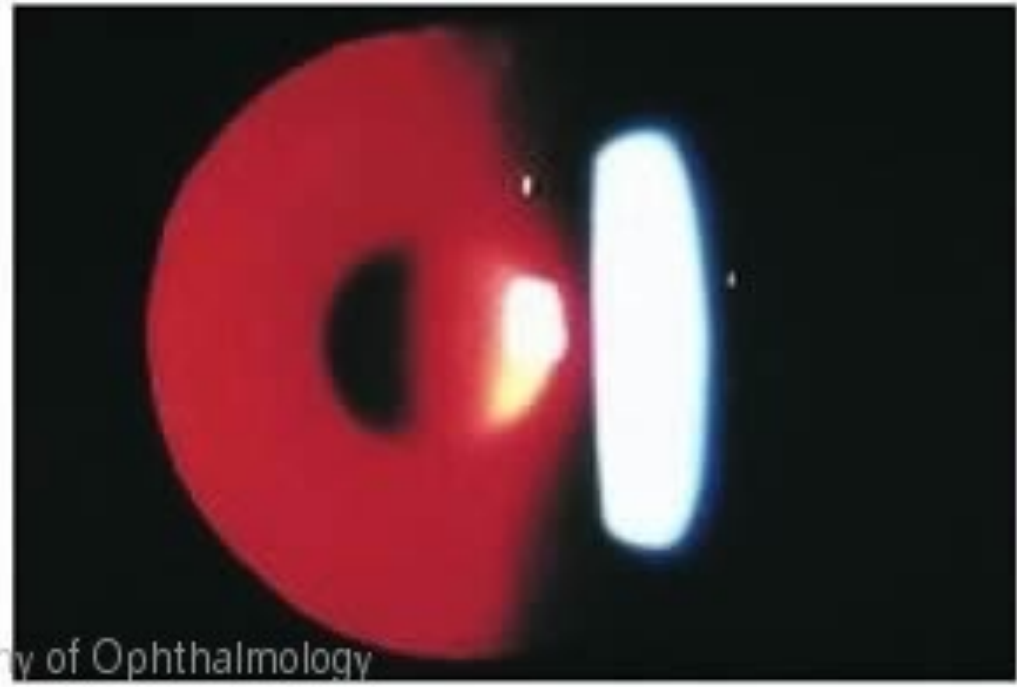
Posterior Lenticonus

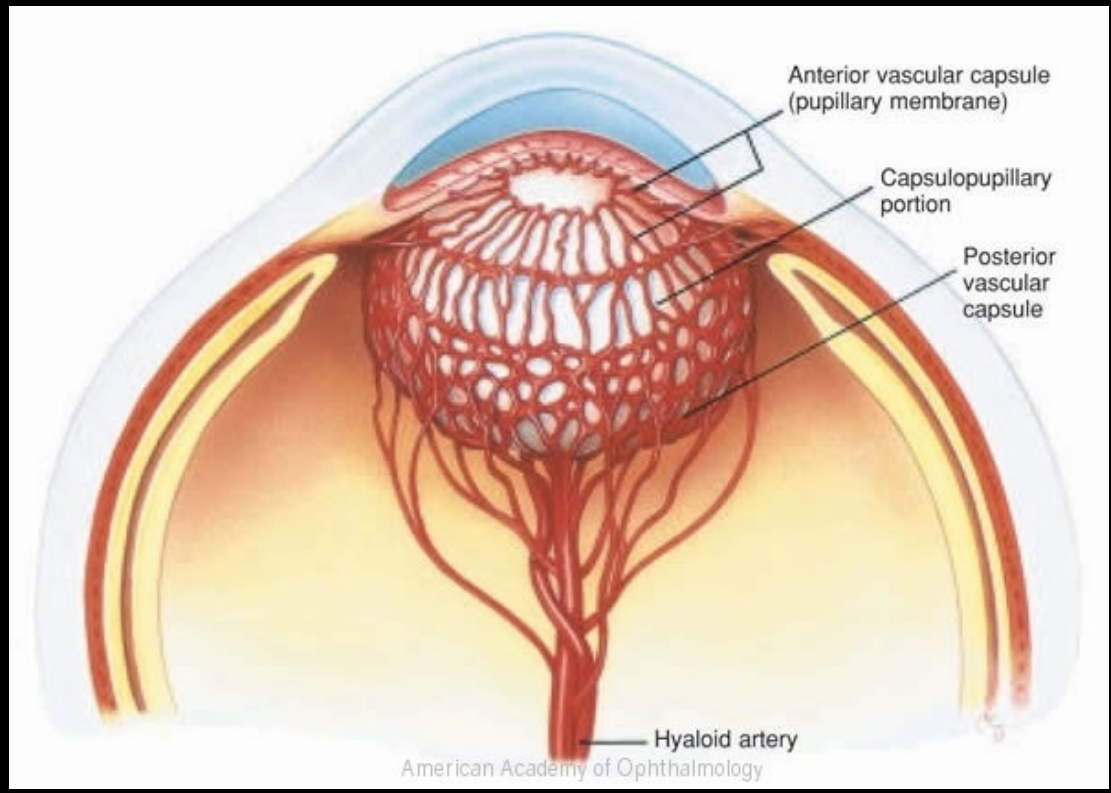
- Bulging of posterior lens capsule
- May be easily identified on dilated retinoscopy
- Cataract is acquired and progressive, usually unilateral
- Anterior lenticonus: Alport syndrome (nephritis, anterior lenticonus and deafness)





Persistent Fetal Vasculature

- Persistent hyperplastic primary vitreous= persistent fetal vasculature
- Anterior and/or Posterior



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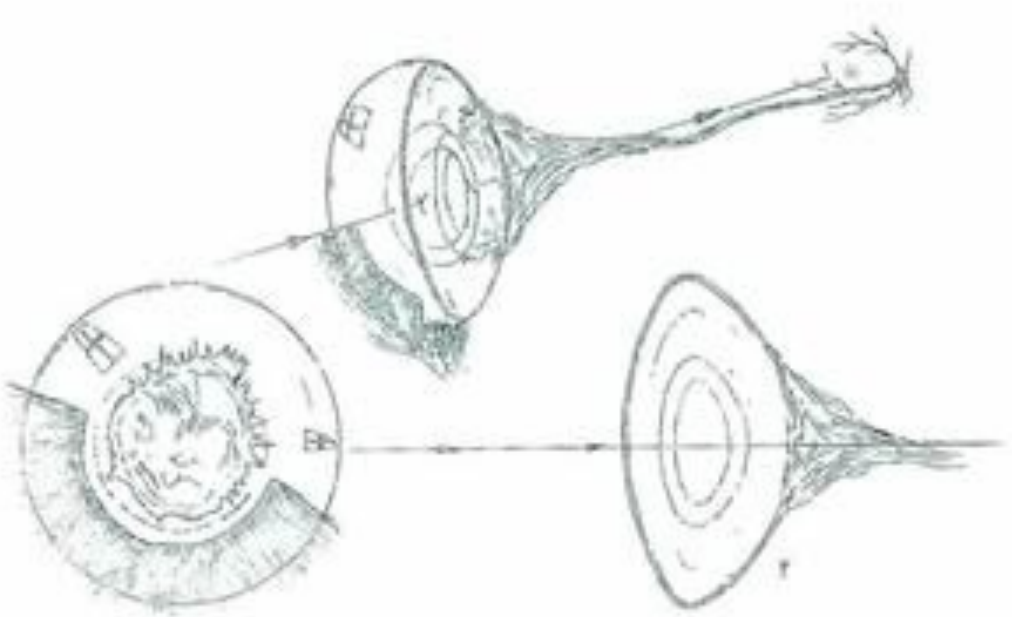
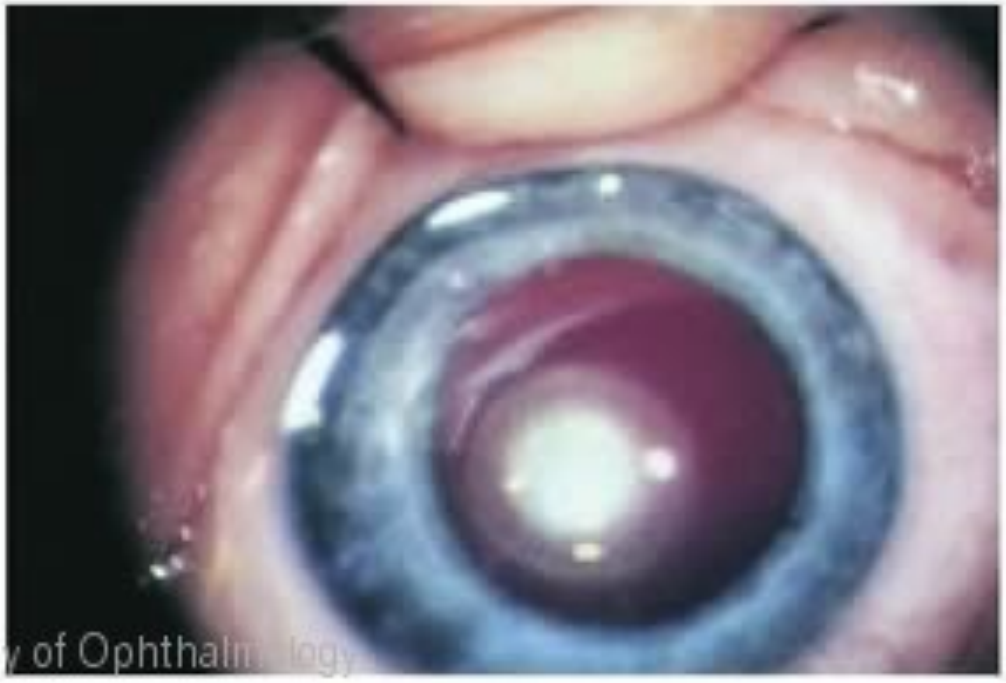
PFV





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PFV

- Ensure retina not involved
- Most eyes microphthalmic
- Posterior lenticular vascular membrane
- Excision of membrane often quite difficult
- Short and long term complications common
  - Secondary membranes
  - Retinal Detachment
  - Glaucoma

Subcapsular (cortical) Cataracts

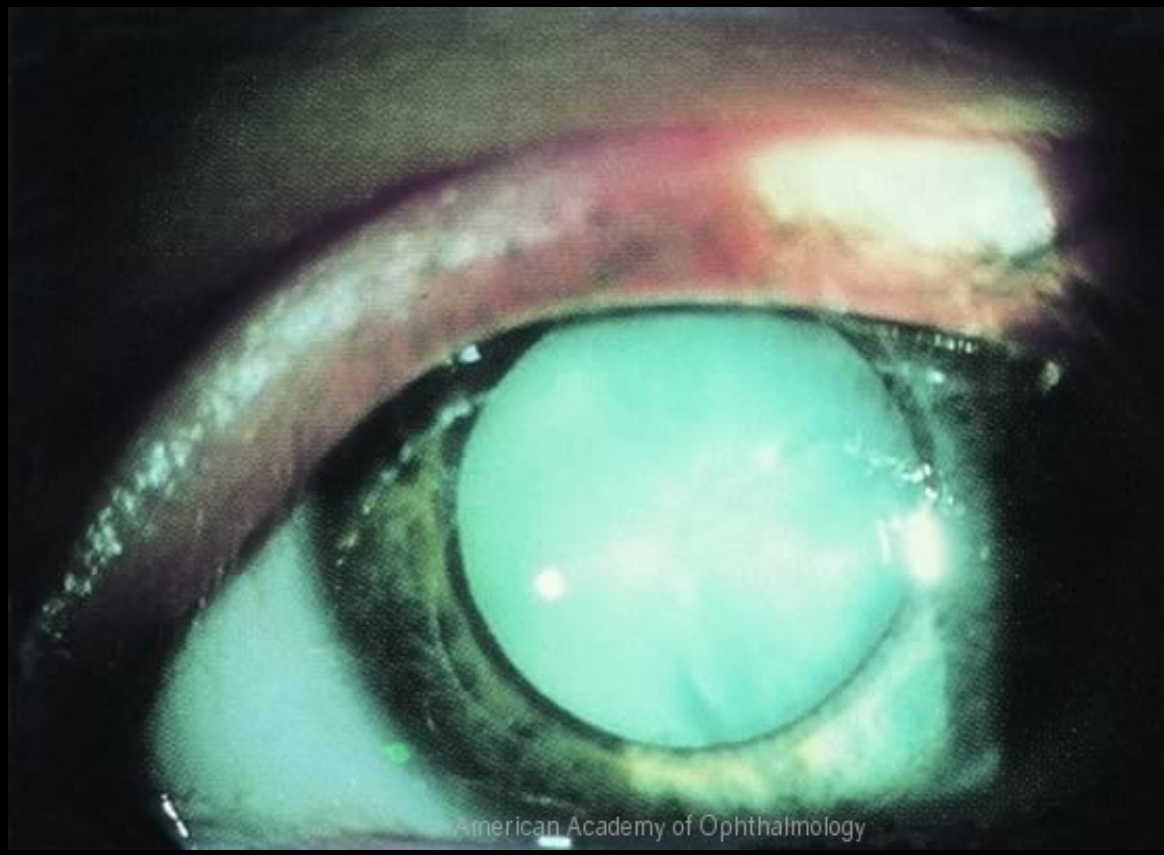
- Anterior subcapsular
  - Associations: Conradi's syndrome (Chrondodysplasia punctata, rhizomelic form usually lethal young)
  - Work up: X-ray of epiphyses of long bones (stippled epiphyses)
- Posterior subcapsular
  - Associations: Diabetes mellitus, corticosteroids, radiation, Refsum's disease, JIA, Retinitis pigmentosa
  - Work up: Fasting blood sugar, Hb A1c, Serum phytanic acid (Refsum's dz), ANA/RF or Peds Rheumatology consult, ERG

Complete Cataract

- Association: Galactosemia from Galactose 1-phosphate uridylyltransferase (GALT) deficiency or Galactokinase deficiency (GALK)
  - Work up: Test urine for reducing substances (Clinitest) screening test, RBC GALT level, RBC galactokinase activity
  - **Also can have “oil droplet” configuration
- Other Associations: Congenital rubella, CMV
  - Work up: rubella IgM and IgG in neonate and mother, TORCH titers, urine culture for CMV

Galactosemia

- Symptoms begin within first few days of life
- Jaundice, vomiting, diarrhea, poor feeding, failure to thrive, lethargy, sepsis
- Cataracts 30%
  - Most mild and resolve with dietary intervention



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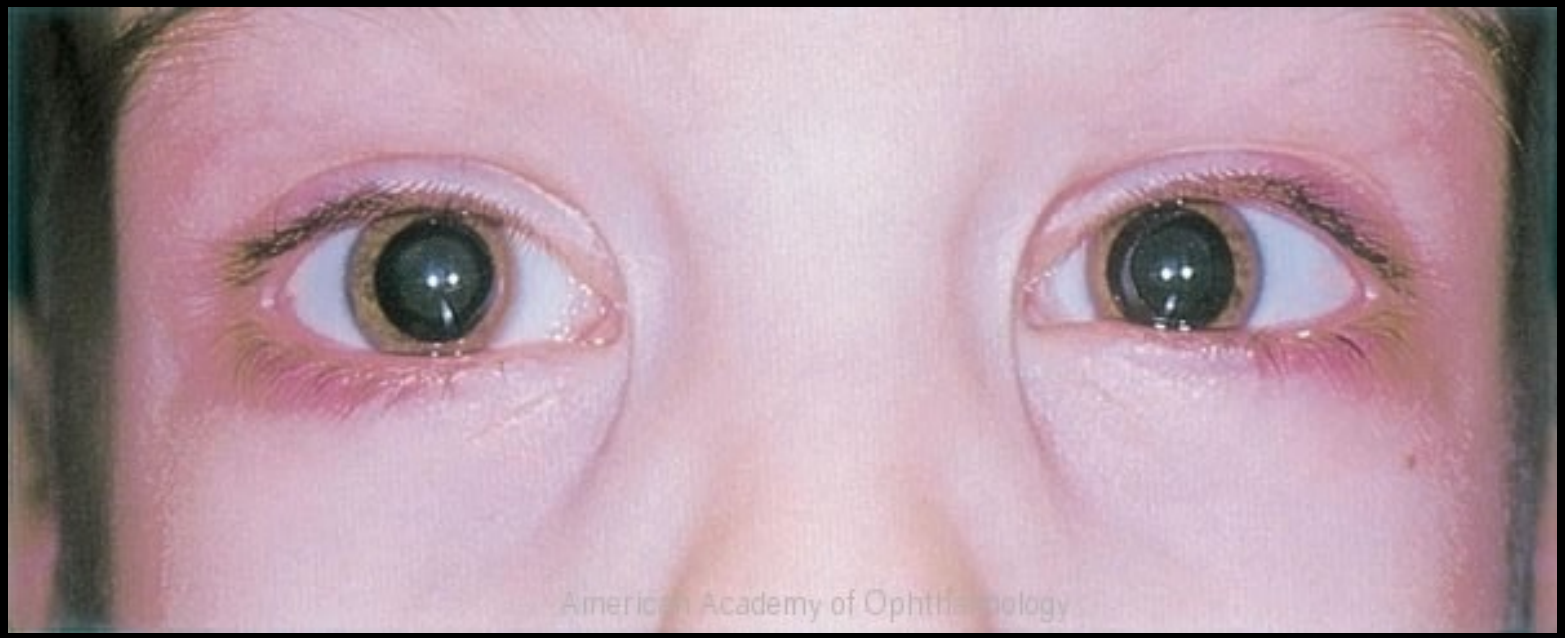
Galactosemia



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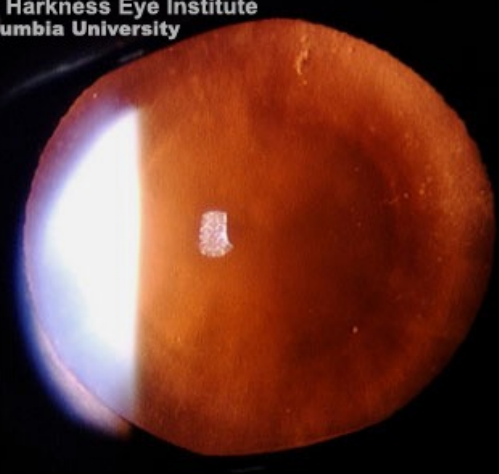

Screening for Metabolic Diseases

- Most states require screening for
  - galactosemia (GALT)
    - PKU, Congenital hypothyroidism, congenital adrenal hyperplasia, Sickle cell disease, hyperphenylalaninemia
  - Most states do not require screening for galactokinase deficiency

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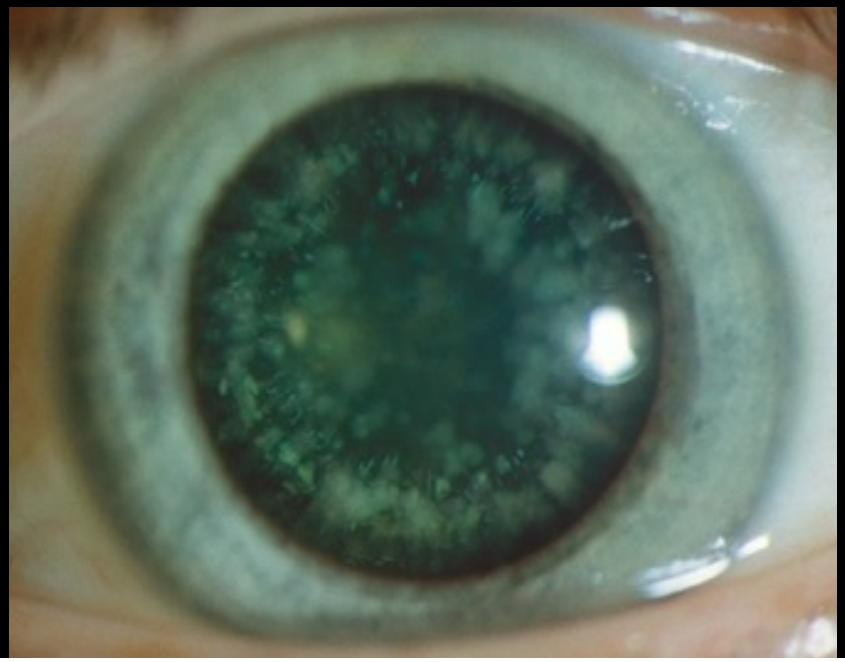
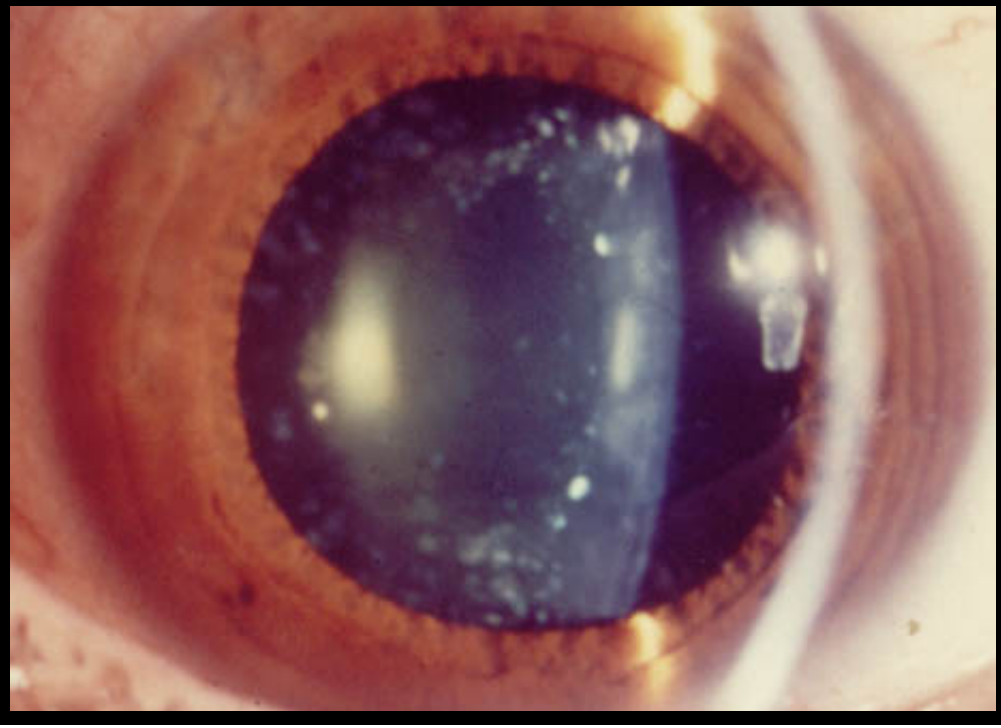
Punctate Cataracts

- Association: Down Syndrome (Cerulean)
- Work up: chromosome analysis
- Less often requires surgery as usually not visually significant





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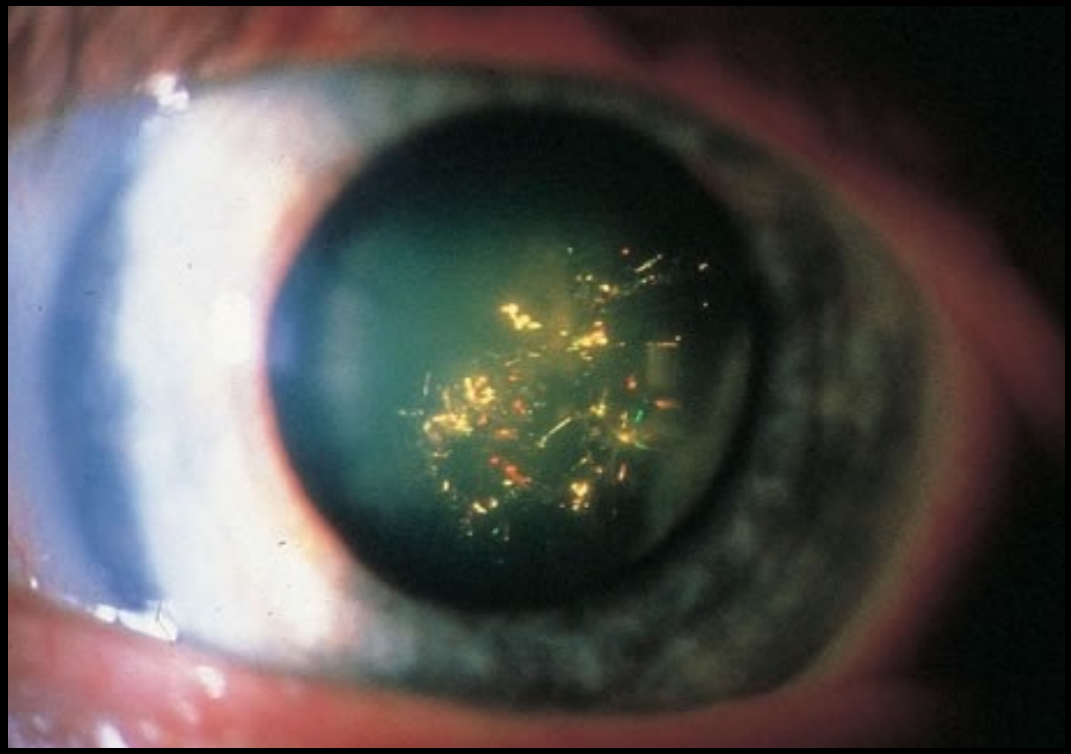
Multicolored flecks

- Associations: myotonic dystrophy
- Work up: Genetic Studies



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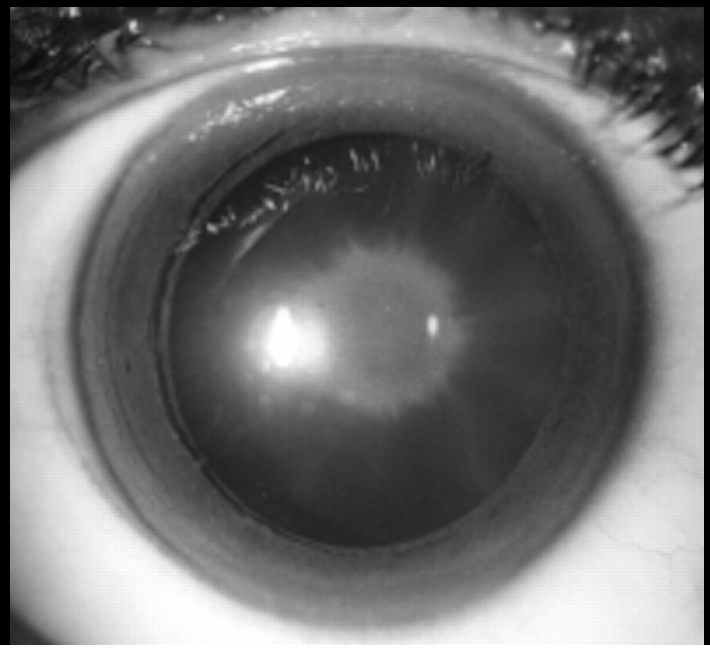
Sunflower Cataract

- Association: Wilson disease
- Work up: Increased serum copper, decreased serum ceruloplasim, elevated 24 hour urinary copper



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Pediatric Cataract Surgery

- Infants should have lensecomy and anterior vitrectomy as soon as possible if older than 4 weeks of age and if cataract is visually significant
- Leave enough lens capsule for future IOL
- Primary IOL implantation in younger than 12 month results in frequent complications

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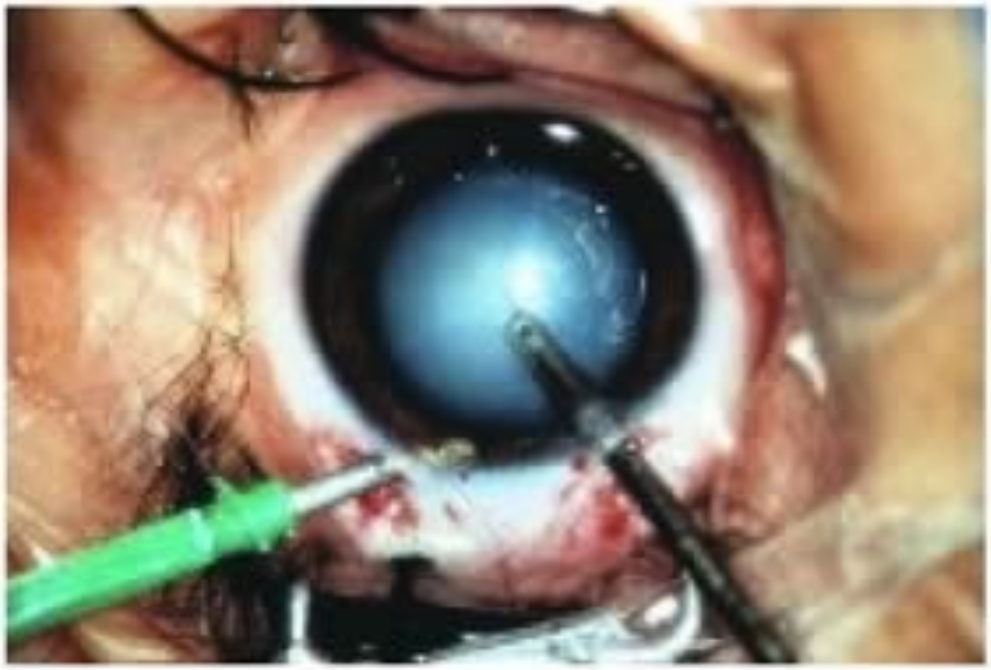
Pediatric Cataract Surgery

- Aphakic glaucoma
  - up to ~30%
  - Correlation with age at time of surgery
    - Esp. <5-6 weeks
- Amblyopia (deprivation, anisometropic)
  - Correlates with age at time of surgery
    - Esp >3 months
- Strabismus (ET)- ~33%



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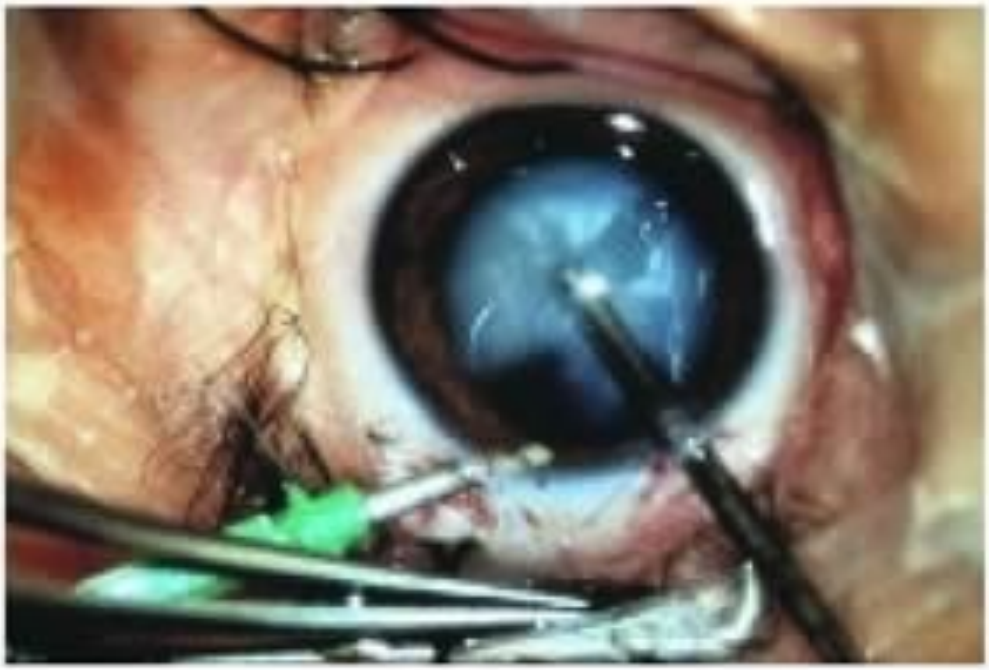

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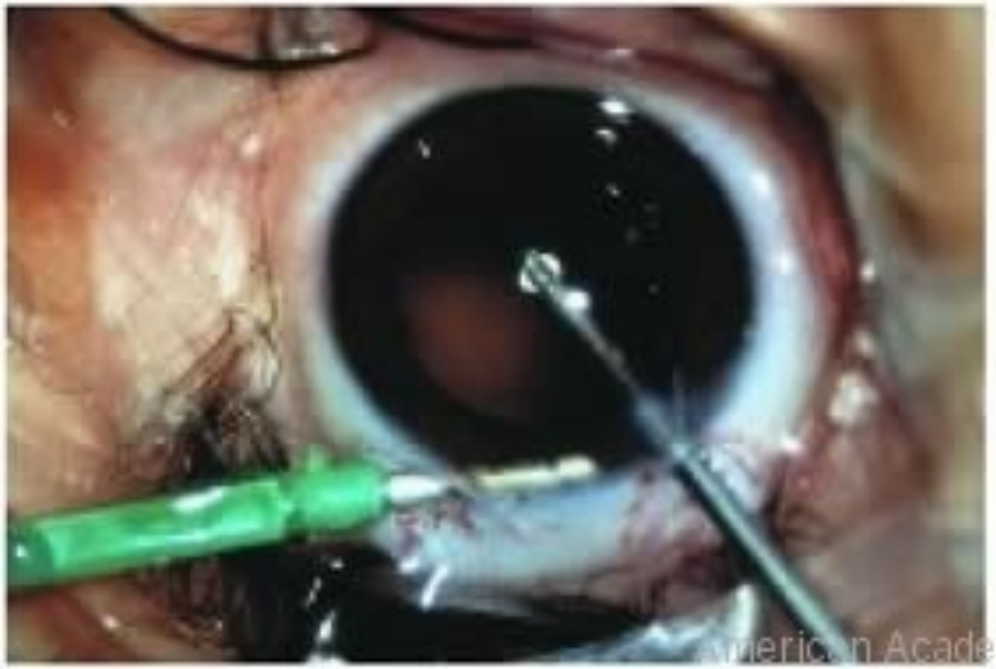

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Pediatric Cataract Visual Rehabilitation

- Aphakic spectacles for bilateral cases in infants
  - Start by over correcting by +1 to 3D for near working distance (over-refaction -1 to -3)
- Contact lenses are most common at UIHC
  - RGP's- with initial induced myopia
- Secondary IOL after age 2
  - Eye has finished most growth
  - If intolerant to current therapy

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Patching in Peds Cataract

Age	Patching Dose
0-2 months	50% Waking Hours
2-7 months	75% Waking Hours
7 months - Subjective Va test	100%- Full Time Patching
Stable Vision to Visual Maturity	FTO or PTO

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Pediatric Cataract Treatment

- Primary IOL
  - Plan on large myopic shift
    - Overcorrection initially will give better long term refractive outcome
    - Overcorrection may make amblyopia treatment more difficult
- IOL calculations: SRK-T

Age	Residual Refraction
<1.9 months	+10 D
2.0-3.9 months	+9 D
4.0-5.9 months	+8 D
6.0-11.9 months	+7 D
1.0-1.9 years	+6 D
2.0-3.9 years	+5 D
4.0-4.9 years	+4 D
5.0-5.9 years	+3 D
6.0-6.9 years	+2 D
7.0-7.9 years	+1.5 D
8.0-9.9 years	+1 D
10.0-13.9 years	+0.5 D
>14 years	Plano

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Pediatric Cataract Treament

- IATS (Infant Aphakia Treatment Study)
  - IOL and Contact lens- same visual acuity
  - More surgeries if IOL implanted

- Acrylic single or 3 piece lenses. PMMA lenses for scleral fixated lens

- If younger than ~5 yrs need to do primary posterior capsulotomy unless YAG available in OR

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